```
=> d his full

     (FILE 'HOME' ENTERED AT 08:25:08 ON 24 JUN 2005)

     FILE 'REGISTRY' ENTERED AT 08:25:33 ON 24 JUN 2005
                ACT AUD807F0/Q
               ---------
L1              STR
               ---------
L2              STR L1
                D QUE L2
L3              SCR 1841
L4              SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 OR 204
L5            0 SEA CSS SAM L2 AND L3 NOT L4

     FILE 'HCAPLUS' ENTERED AT 08:30:49 ON 24 JUN 2005
L6            1 SEA ABB=ON  PLU=ON  (GB99-17793# OR WO2000-GB2903#)/AP,RPN

     FILE 'REGISTRY' ENTERED AT 08:32:01 ON 24 JUN 2005

     FILE 'HCAPLUS' ENTERED AT 08:32:03 ON 24 JUN 2005
L7              TRA L6 1- RN :        65 TERMS

     FILE 'REGISTRY' ENTERED AT 08:32:03 ON 24 JUN 2005
L8           65 SEA ABB=ON  PLU=ON  L7
L9           16 SEA ABB=ON  PLU=ON  L8 AND NR>=4
L10      256861 SEA ABB=ON  PLU=ON  C5-C6-C6-C6/ES
L11             STR L2
L12          35 SEA SUB=L10 CSS SAM L11 AND L3 NOT L4
L13           0 SEA SUB=L10 CSS SAM L2 AND L3 NOT L4
L14        4008 SEA SUB=L10 CSS FUL L11 AND L3 NOT L4
                D QUE L2
L15           4 SEA SUB=L14 SSS SAM L2
                D SCA
L16         106 SEA SUB=L14 SSS FUL L2
                SAV TEM L14 AUD807F0/A
                SAV TEM L16 AUD807S0/A

     FILE 'HCAPLUS' ENTERED AT 08:44:01 ON 24 JUN 2005
                E MORRISON J/AU
L17         246 SEA ABB=ON  PLU=ON  ("MORRISON J"/AU OR "MORRISON J D"/AU)
                E MORRISON JAMES/AU
L18          22 SEA ABB=ON  PLU=ON  ("MORRISON JAMES"/AU OR "MORRISON JAMES
                DUNCAN"/AU)
                E MORRISON JIM/AU
L19           4 SEA ABB=ON  PLU=ON  "MORRISON JIM"/AU
                E LUCAS M/AU
L20         190 SEA ABB=ON  PLU=ON  ("LUCAS M"/AU OR "LUCAS M L"/AU)
                E LUCAS MIKE/AU
                E LUCAS MICHAEL/AU
L21          17 SEA ABB=ON  PLU=ON  ("LUCAS MICHAEL"/AU OR "LUCAS MICHAEL
                L"/AU OR "LUCAS MICHAEL LESLIE"/AU)
                E WHEELER S/AU
L22          56 SEA ABB=ON  PLU=ON  ("WHEELER S"/AU OR "WHEELER S A"/AU OR
                "WHEELER S C"/AU OR "WHEELER S E"/AU OR "WHEELER S F"/AU OR
                "WHEELER S G"/AU OR "WHEELER S H"/AU OR "WHEELER S J"/AU OR
                "WHEELER S JAMES"/AU OR "WHEELER S L"/AU OR "WHEELER S M"/AU
                OR "WHEELER S R"/AU OR "WHEELER S S"/AU OR "WHEELER S T"/AU OR
                "WHEELER S V"/AU)
                E WHEELER SARAH/AU
L23          16 SEA ABB=ON  PLU=ON  ("WHEELER SARAH"/AU OR "WHEELER SARAH
                C"/AU OR "WHEELER SARAH CAROLINE"/AU OR "WHEELER SARAH E"/AU
                OR "WHEELER SARAH J"/AU OR "WHEELER SARAH L"/AU)
L24          90 SEA ABB=ON  PLU=ON  L16
L25             QUE ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS+OLD,NT/CT
L26           0 SEA ABB=ON  PLU=ON  L24 AND L25
```

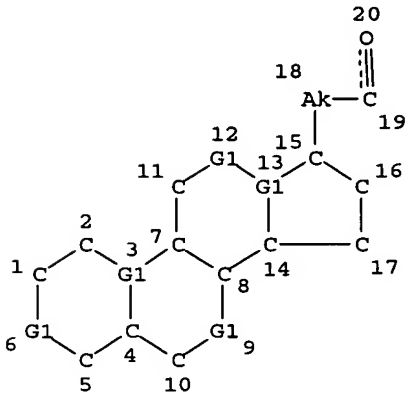
Search done by Noble Jarrell

```
L27           8 SEA ABB=ON  PLU=ON  L24 AND ?CONJUGAT?
L28           0 SEA ABB=ON  PLU=ON  L16/D
L29           0 SEA ABB=ON  PLU=ON  L24 AND (L17 OR L18 OR L19 OR L20 OR L21
                OR L22)
L30           5 SEA ABB=ON  PLU=ON  L14 AND (L17 OR L18 OR L19 OR L20 OR L21
                OR L22)
L31       17638 SEA ABB=ON  PLU=ON  L14 NOT L30
L32        2551 SEA ABB=ON  PLU=ON  L31 AND ?CONJUGAT?
L33         134 SEA ABB=ON  PLU=ON  L32 AND L25
L34             QUE ABB=ON  PLU=ON  PY<=1999 OR AY<=1999 OR PRY<=1999 OR
                PD<19990730 OR AD<19990730 OR PRD<19990730
L35          64 SEA ABB=ON  PLU=ON  L33 AND L34
L36           7 SEA ABB=ON  PLU=ON  L27 AND L34
L37           8 SEA ABB=ON  PLU=ON  L27 OR L36
                SEL AN L35 4 5 11 16 18 20-21 25 29 31-33 43-44 48 50
L38          16 SEA ABB=ON  PLU=ON  ("119:146497"/AN OR "120:173477"/AN OR
                "121:286635"/AN OR "123:322102"/AN OR "126:308684"/AN OR
                "126:347323"/AN OR "127:99659"/AN OR "128:286354"/AN OR
                "130:213559"/AN OR "131:314185"/AN OR "132:26813"/AN OR
                "132:313463"/AN OR "132:73648"/AN OR "133:140227"/AN OR
                "136:107571"/AN OR "136:665"/AN OR "1993:546497"/AN OR
                "1994:173477"/AN OR "1994:686635"/AN OR "1995:721131"/AN OR
                "1997:218959"/AN OR "1997:372273"/AN OR "1997:463447"/AN OR
                "1998:208387"/AN OR "1999:185918"/AN OR "1999:708452"/AN OR
                "1999:722480"/AN OR "1999:764076"/AN OR "2000:10612"/AN OR
                "2000:508917"/AN OR "2001:844884"/AN OR "2002:72799"/AN) AND
                L35
                SEL AN 1 2 5 8 16 L38
L39          11 SEA ABB=ON  PLU=ON  L38 NOT ("119:146497"/AN OR "130:213559"/AN
                 OR "132:26813"/AN OR "136:107571"/AN OR "136:665"/AN OR
                "1993:546497"/AN OR "1999:185918"/AN OR "1999:764076"/AN OR
                "2001:844884"/AN OR "2002:72799"/AN)
L40          19 SEA ABB=ON  PLU=ON  L37 OR L39

     FILE 'EMBASE' ENTERED AT 09:22:40 ON 24 JUN 2005
L41           0 SEA ABB=ON  PLU=ON  L16
L42       11483 SEA ABB=ON  PLU=ON  L14
L43        1146 SEA ABB=ON  PLU=ON  L42 AND ?CONJUGAT?
                E ORAL/CT
                E E5+ALL
                E E2+ALL
L44         109 SEA ABB=ON  PLU=ON  ORAL DRUG ADMINISTRATION/CT AND L43
                E MORRISON J/AU
L45         338 SEA ABB=ON  PLU=ON  ("MORRISON J"/AU OR "MORRISON J D"/AU)
                E MORRISON JIM/AU
                E MORRISON JAMES/AU
                E LUCAS M/AU
L46         326 SEA ABB=ON  PLU=ON  ("LUCAS M"/AU OR "LUCAS M L"/AU)
                E LUCAS MICHAEL/AU
                E WHEELER S/AU
L47         151 SEA ABB=ON  PLU=ON  ("WHEELER S"/AU OR "WHEELER S A"/AU OR
                "WHEELER S B"/AU OR "WHEELER S C"/AU OR "WHEELER S D"/AU OR
                "WHEELER S E"/AU OR "WHEELER S F"/AU OR "WHEELER S G"/AU OR
                "WHEELER S H"/AU OR "WHEELER S J"/AU OR "WHEELER S K"/AU OR
                "WHEELER S L"/AU OR "WHEELER S M"/AU OR "WHEELER S R"/AU OR
                "WHEELER S V"/AU OR "WHEELER S W"/AU)
L48           4 SEA ABB=ON  PLU=ON  L42 AND (L45 OR L46 OR L47)
L49         109 SEA ABB=ON  PLU=ON  L44 NOT L48
L50          91 SEA ABB=ON  PLU=ON  L49 AND PY<=1999

     FILE 'EMBASE' ENTERED AT 09:33:50 ON 24 JUN 2005
                SEL AN L50 60 63 40 43 46 12 16 20 29 2 3 5
L51          12 SEA ABB=ON  PLU=ON  (1999046272/AN OR 1999256785/AN OR
                1999324376/AN OR 84147710/AN OR 85080967/AN OR 88276787/AN OR
                89150062/AN OR 90226900/AN OR 92292458/AN OR 94299511/AN OR
                95240331/AN OR 96132330/AN) AND L50
```

Search done by Noble Jarrell

```
     FILE 'BIOSIS' ENTERED AT 09:34:08 ON 24 JUN 2005
L52         9899 SEA ABB=ON  PLU=ON  L14 OR L16
L53         1104 SEA ABB=ON  PLU=ON  L52 AND ?CONJUGAT?
                 E MORRISON J/AU
L54          392 SEA ABB=ON  PLU=ON  ("MORRISON J"/AU OR "MORRISON J D"/AU)
                 E MORRISON JAMES/AU
L55            4 SEA ABB=ON  PLU=ON  ("MORRISON JAMES"/AU OR "MORRISON JAMES
                 D"/AU)
                 E M LUCAS M/AU
                 E LUCAS M/AU
L56          280 SEA ABB=ON  PLU=ON  ("LUCAS M"/AU OR "LUCAS M L"/AU)
                 E LUCAS MICHAEL/AU
L57            3 SEA ABB=ON  PLU=ON  ("LUCAS MICHAEL"/AU OR "LUCAS MICHAEL
                 L"/AU)
                 E WHEELER S/AU
L58          160 SEA ABB=ON  PLU=ON  ("WHEELER S"/AU OR "WHEELER S A"/AU OR
                 "WHEELER S C"/AU OR "WHEELER S CHRISTIAN"/AU OR "WHEELER S
                 D"/AU OR "WHEELER S E"/AU OR "WHEELER S F"/AU OR "WHEELER S
                 G"/AU OR "WHEELER S G B"/AU OR "WHEELER S H"/AU OR "WHEELER S
                 J"/AU OR "WHEELER S JAMES"/AU OR "WHEELER S K"/AU OR "WHEELER
                 S L"/AU OR "WHEELER S M"/AU OR "WHEELER S P"/AU OR "WHEELER S
                 R"/AU OR "WHEELER S V"/AU OR "WHEELER S W"/AU)
                 E WHEELER SARA/AU
L59           21 SEA ABB=ON  PLU=ON  ("WHEELER SARAH"/AU OR "WHEELER SARAH
                 C"/AU OR "WHEELER SARAH E"/AU OR "WHEELER SARAH L"/AU OR
                 "WHEELER SCHILLING T"/AU)
L60            1 SEA ABB=ON  PLU=ON  L53 AND (L54 OR L55 OR L56 OR L57 OR L58
                 OR L59)

=> b reg
FILE 'REGISTRY' ENTERED AT 09:38:18 ON 24 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   23 JUN 2005  HIGHEST RN 852898-09-0
DICTIONARY FILE UPDATES:  23 JUN 2005  HIGHEST RN 852898-09-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*************************************************************************
*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que sta l14
```

L3 SCR 1841
L4 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 O
R 2043 OR 2054
L10 256861 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES
L11 STR



C—OH @21 22
C—Ak @23 24

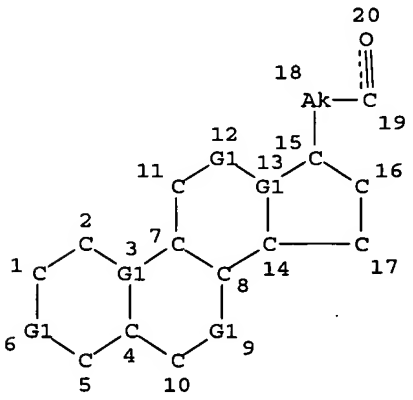
VAR G1=C/21/23
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 19
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L14 4008 SEA FILE=REGISTRY SUB=L10 CSS FUL L11 AND L3 NOT L4

100.0% PROCESSED 201370 ITERATIONS 4008 ANSWERS
SEARCH TIME: 00.00.10

=> d que sta l16
L2 STR

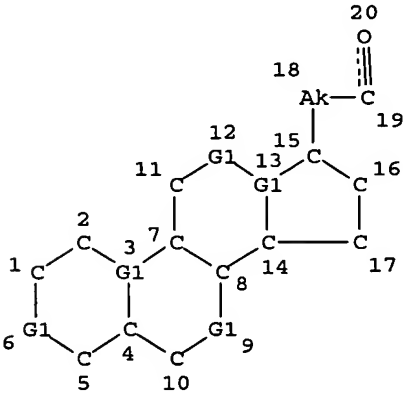


C—OH @21 22
C—Ak @23 24

VAR G1=C/21/23
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 19
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 18
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L3 SCR 1841
L4 SCR 2039 OR 2041 OR 2050 OR 2049 OR 2053 OR 2052 OR 2048 O
R 2043 OR 2054
L10 256861 SEA FILE=REGISTRY ABB=ON PLU=ON C5-C6-C6-C6/ES
L11 STR



C—OH @21 22
C—Ak @23 24

VAR G1=C/21/23
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 19
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
L14 4008 SEA FILE=REGISTRY SUB=L10 CSS FUL L11 AND L3 NOT L4
L16 106 SEA FILE=REGISTRY SUB=L14 SSS FUL L2

100.0% PROCESSED 4008 ITERATIONS 106 ANSWERS
SEARCH TIME: 00.00.01

=> b hcap
FILE 'HCAPLUS' ENTERED AT 09:38:45 ON 24 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 24 Jun 2005 VOL 143 ISS 1
FILE LAST UPDATED: 23 Jun 2005 (20050623/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

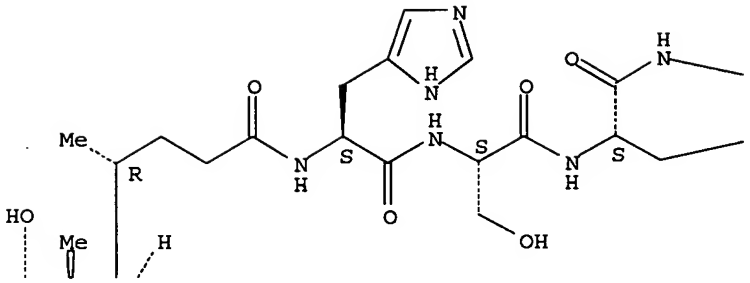
=> d all fhitstr l30 tot

L30 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:394158 HCAPLUS
DN 141:47626
ED Entered STN: 14 May 2004
TI Absorption of the cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo
AU McHarg, S.; Morton, J. S.; McGinn, B. J.; Yasin, M.; **Morrison, J. D.**
CS Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK
SO Acta Physiologica Scandinavica (2004), 181(1), 23-34
CODEN: APSCAX; ISSN: 0001-6772
PB Blackwell Publishing Ltd.
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
AB Previously, the authors demonstrated that gastrin peptides as long as 34 amino acids were absorbed from the ileum of rat after conjugation to the C24 position of cholic acid and that these peptides retained full biol. activity. As absorption was specific to the ileum, it was inferred that the conjugated hormone was taken up by the bile salt transporters. The authors have now extended these expts. to a member of a different family of hormones, viz. secretin, a 27-amino acid hormone that stimulates serous secretions from the exocrine pancreas. After conjugation to cholic acid, the degree of cholylsecretin absorption from the ileum of anesthetized rats was assessed from the increase in pancreatic secretions. A complication to the study was that intra-ileal infusion of native secretin caused a transient increase in the levels of pancreatic secretions. This was in contrast to the effects of intra-ileal infusion of cholylsecretin which did not cause this transient increase but, instead, gave rise to a delayed increase in pancreatic secretions which was sustained over several hours during which cholylsecretin was detected in plasma in high concentration by mass spectrometry. The pancreatic response to cholylsecretin was abolished by co-infusion of 50 mM taurocholate, employed to compete with the bile salt transporters, although a transient increase in pancreatic secretions similar to that caused by secretin was now generated. This was shown to arise from an action of taurocholate per se causing the release of endogenous secretin which is present in rat ileum. The authors, therefore, concluded that cholylsecretin had been absorbed from the rat ileum by uptake by bile salt transporters.
ST secretin cholic acid conjugate bile salt absorption ileum rat; cholylsecretin absorption bile salt transporter ileum
IT Pancreas
(absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bile salt; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
IT Intestine
(ileum; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
IT Bile salts
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transporter; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
IT Biological transport
(uptake; absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)

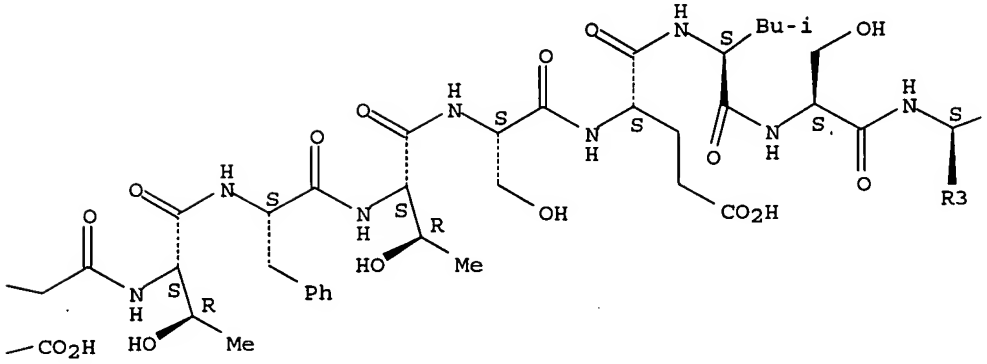
IT 71-52-3, Bicarbonate, biological studies **709002-71-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Baker, R; Proc Soc Exp Biol Med 1960, V105, P521 HCAPLUS
(2) Bayliss, W; J Physiol 1902, V28, P325 HCAPLUS
(3) Bodanszky, A; J Am Chem Soc 1969, V91, P944 HCAPLUS
(4) Chey, W; J Physiol 1982, V324, P263 HCAPLUS
(5) Dakka, T; Digestion 1995, V56, P165 HCAPLUS
(6) Dietschy, J; J Lipid Res 1968, V9, P297 HCAPLUS
(7) Gossen, D; Biochem Biophys Res Commun 1989, V160, P862 HCAPLUS
(8) Gourlet, P; Eur J Biochem 1996, V239, P349 HCAPLUS
(9) Gourlet, P; Peptides 1996, V17, P825 HCAPLUS
(10) Gronenborn, A; FEBS Lett 1987, V215, P88 HCAPLUS
(11) Horvath, K; J Assoc Acad Min Phys 1998, V9, P9 MEDLINE
(12) Izzo, R; Int J Pept Prot Res 1984, V23, P292 HCAPLUS
(13) Jin, H; Gastroenterology 1993, V105, P208 HCAPLUS
(14) Kern, J; J Autism Develop Disord 2002, V32, P153
(15) Larsson, L; Histochemistry 1978, V58, P23 HCAPLUS
(16) Morely, J; Nature 1965, V207, P1356
(17) Moriyasu, M; Pancreas 1994, V9, P129 MEDLINE
(18) Morrison, J; J Physiol Proceedings 2004
(19) New, R; Int Patent Appl WO 96/06635 1996
(20) O'Maille, E; J Physiol 1965, V180, P67 HCAPLUS
(21) Playoust, M; J Clin Invest 1964, V43, P467 HCAPLUS
(22) Roberts, P; Digestion 1999, V60, P332 HCAPLUS
(23) Straus, E; Gastroenterology 1978, V75, P401 HCAPLUS
(24) The Diabetes Control And Complications Trial Research Group; New Engl J Med 2000, V342, P381
(25) Tranberg, K; Ann Surg 1985, V201, P300 HCAPLUS
(26) Weiner, I; Handbook of Physiology - Alimentary Canal III 1967, P1439
(27) Wettergren, A; Digest Dis Sci 1993, V38, P665 HCAPLUS
(28) Wheeler, S; Acta Physiol Scand 2002, V176, P203 HCAPLUS
(29) Wheeler, S; Exp Physiol 1997, V82, P729 HCAPLUS
IT **709002-71-1**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption of cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo)
RN 709002-71-1 HCAPLUS
CN L-Valinamide, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-histidyl-L-seryl-L-α-aspartylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-glutamyl-L-leucyl-L-seryl-L-arginyl-L-leucyl-L-arginyl-L-α-glutamylglycyl-L-alanyl-L-arginyl-L-leucyl-L-glutaminyl-L-arginyl-L-leucyl-L-leucyl-L-glutaminylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

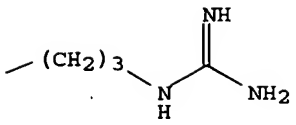
PAGE 1-A



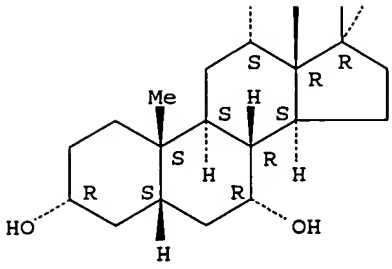
PAGE 1-B

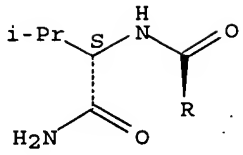


PAGE 1-C

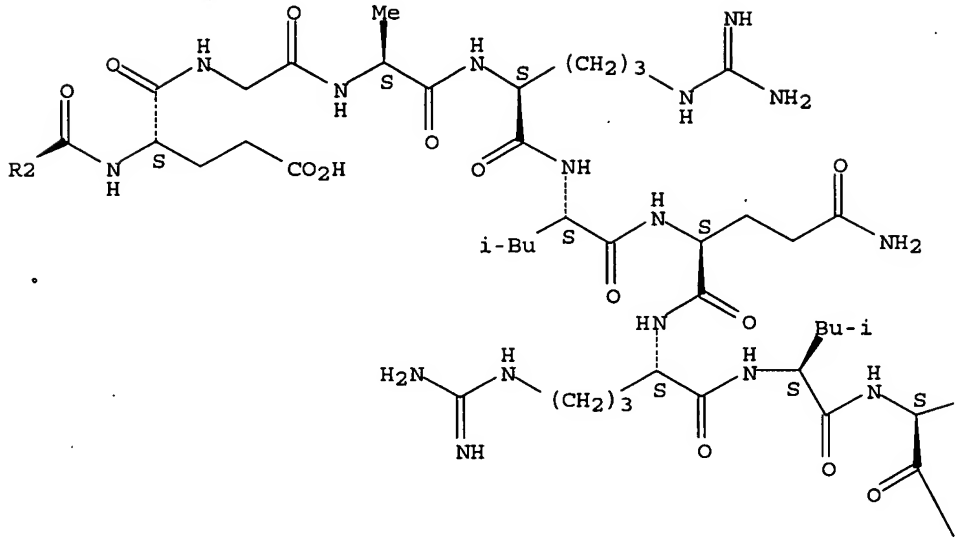


PAGE 2-A





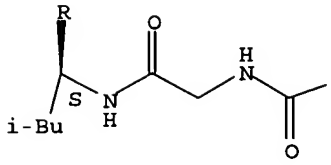
PAGE 3-A

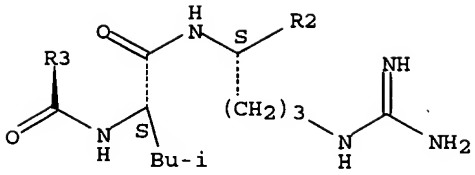


Search done by Noble Jarrell

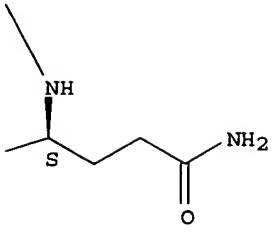
PAGE 3-B

PAGE 4-A





PAGE 4-B



Search done by Noble Jarrell

L30 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:869795 HCAPLUS
DN 138:181158
ED Entered STN: 17 Nov 2002
TI Absorption of biologically active peptide hormones from the small intestine of rat
AU **Wheeler, S.**; McGinn, B. J.; **Lucas, M. L.**; **Morrison, J. D.**
CS University of Glasgow, Glasgow, G12 8QQ, UK
SO Acta Physiologica Scandinavica (2002), 176(3), 203-213
CODEN: APSCAX; ISSN: 0001-6772
PB Blackwell Science Ltd.
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amount of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each of the forms of gastrin was conjugated at the free N-terminus to the carboxyl group of cholic acid. Subsequent infusion of the conjugated form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addition, conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to i.v. injection of the hormone. Absorption of the gastrin conjugates was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.
ST gastrin isoform absorption small intestine rat
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bile salt; absorption of biol. active peptide hormones from ileum of rat indicates absorption through bile salt transporters)
IT Intestine
(ileum; absorption of biol. active peptide hormones from the small intestine of rat)
IT Gastric acid
(secretion; absorption of biol. active peptide hormones from the small intestine of rat)
IT Circulation
(systemic; absorption of biol. active peptide hormones from the small intestine of rat)
IT Bile salts
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transporter; absorption of biol. active peptide hormones from ileum of rat indicates absorption through bile salt transporters)
IT Biological transport
(uptake; absorption of biol. active peptide hormones from the small intestine of rat)
IT 1947-37-1, 4-7-Cholecystokinin-7 (swine) 18828-47-2 **171511-54-9** **324753-46-0** **496946-81-7** 499210-69-4 499210-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption of biol. active peptide hormones from the small intestine of rat)
IT **81-25-4**, Cholic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(conjugate; absorption of biol. active peptide hormones from the small intestine of rat)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Baker, R; Proc Soc Exp Biol Med 1960, V105, P521 HCAPLUS

(2) Bendayan, M; Diabetologica 1990, V33, P197 HCAPLUS
(3) Burkoth, T; Crit Rev Therap Drug Carr Sys 1999, V16, P331 HCAPLUS
(4) Chan, W; Fmoc Solid Phase Peptide Synthesis -- a Practical Approach 2000
(5) Dakka, T; Digestion 1995, V56, P165 HCAPLUS
(6) Damge, C; J Pharmaceut Sci 1997, V86, P1403 HCAPLUS
(7) Davenport, H; Physiology of the Digestive Tract, 4th edn 1977
(8) Haas, S; Vaccine 1996, V14, P785 HCAPLUS
(9) Holt, P; Am J Physiol 1964, V207, P1 HCAPLUS
(10) Kramer, W; US 5462933 1995 HCAPLUS
(11) Kramer, W; J Biol Chem 1994, V269, P10621 HCAPLUS
(12) Krchnak, V; Int J Pept Prot Res 1988, V32, P415 HCAPLUS
(13) Lack, L; Am J Physiol 1961, V200, P313 HCAPLUS
(14) Lack, L; Am J Physiol 1966, V210, P1142 HCAPLUS
(15) Layer, P; Digest Dis Sci 1995, V40, P1074 HCAPLUS
(16) Lichteberger, L; Gastroenterology 1986, V90, P1223
(17) Mathlowitz, E; Nature 1997, V386, P410
(18) Matthews, D; Gastroenterology 1976, V71, P151 HCAPLUS
(19) McGinn, B; Proteins Labfax 1996, P139 HCAPLUS
(20) Morley, J; Nature 1965, V207, P1356 HCAPLUS
(21) Muranishi, S; J Contr Release 1992, V19, P179 HCAPLUS
(22) Namba, M; Regul Pept 1986, V15, P121 HCAPLUS
(23) Playoust, M; J Clin Invest 1964, V43, P467 HCAPLUS
(24) Ritschel, W; Meth Find Exp Clin Pharmacol 1991, V13, P205 HCAPLUS
(25) Roberts, P; Digestion 1999, V60, P332 HCAPLUS
(26) Royal Pharmaceutical Society; British National Formulary 2001
(27) Skyler, J; Lancet 2001, V357, P331 HCAPLUS
(28) Stephan, Z; Biochem Pharmacol 1992, V43, P1969 HCAPLUS
(29) Swaan, P; Adv Drug Del Rev 1996, V20, P59 HCAPLUS
(30) Swaan, P; Bioconj Chem 1997, V8, P520 HCAPLUS
(31) Trier, J; Gastroenterol Clin N Am 1991, V20, P531 MEDLINE
(32) Walsh, J; Gut Peptides: Biochemisty and Physiology 1994, P75 HCAPLUS
(33) Weiner, I; Handbook of Physiology -- Alimentary Canal 1967, VIII, P1439
(34) Wheeler, S; Exp Physiol 1997, V82, P729 HCAPLUS

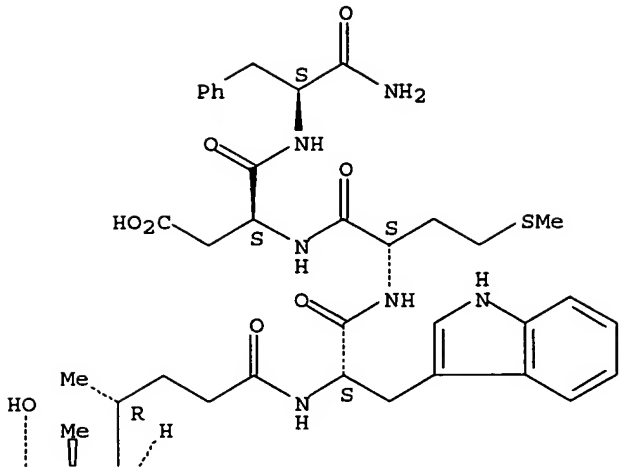
IT **171511-54-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(absorption of biol. active peptide hormones from the small intestine of rat)

RN 171511-54-9 HCAPLUS

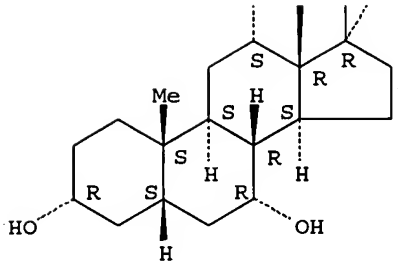
CN L-Phenylalaninamide, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-tryptophyl-L-methionyl-L-α-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

PAGE 1-A



PAGE 2-A



L30 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:101167 HCAPLUS
DN 134:168315
ED Entered STN: 09 Feb 2001
TI Enhancement of bioavailability of peptides with bile salts
IN **Morrison, James Duncan; Lucas, Michael Leslie;**
Wheeler, Sarah
PA The University Court of the University of Glasgow, UK
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001009163	A2	20010208	WO 2000-GB2903	20000728
	WO 2001009163	A3	20010907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2355009 A1 20010411 GB 1999-17793 19990730
AU 2000061739 A5 20010219 AU 2000-61739 20000728
EP 1228093 A2 20020807 EP 2000-948177 20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI GB 1999-17793 A 19990730
WO 2000-GB2903 W 20000728

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001009163	ICM	C07J
WO 2001009163	ECLA	A61K047/48H4; C07K014/47; C07K014/575; C07K014/595
GB 2355009	ECLA	A61K047/48H4; C07K014/47; C07K014/575; C07K014/595

OS MARPAT 134:168315

AB The present invention relates to improving and/or increasing the bioavailability of a biol. active substance, such as a peptide. In particular the present invention relates to the conjugation of the biol. active substance to a bile acid. The conjugated biol. active substance is suitable particularly for oral or parental administration. Illeal administration of 600μg/kg gastrin tetrapeptide conjugated to cholate resulted in a significant mean increase in gastric acid secretion of 1.84 μmol over a 3 h collection period, while no increase in acid secretion was noticed by administration of tetragastrin alone or with sep. cholate.

ST bioavailability enhancement peptide bile salt

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; enhancement of bioavailability of peptides with bile salts)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D; enhancement of bioavailability of peptides with bile salts)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E; enhancement of bioavailability of peptides with bile salts)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G; enhancement of bioavailability of peptides with bile salts)

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M; enhancement of bioavailability of peptides with bile salts)

IT Chemotherapy
(agents; enhancement of bioavailability of peptides with bile salts)

IT Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; enhancement of bioavailability of peptides with bile salts)

IT Anemia (disease)
(antianemic factors; enhancement of bioavailability of peptides with bile salts)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(conjugates; enhancement of bioavailability of peptides with bile salts)

IT Adrenoceptor agonists
Adrenoceptor antagonists
Analgesics
Anesthetics
Anti-inflammatory agents
Antianginal agents
Antiarrhythmics
Antibacterial agents
Anticoagulants
Anticonvulsants
Antidepressants
Antihistamines
Antiparkinsonian agents
Antipsychotics
Antiviral agents
Anxiolytics
Cardiotonics
Diuretics
Drug bioavailability
Fungicides
Hypnotics and Sedatives
Hypolipemic agents
Muscarinic agonists
Muscarinic antagonists
Nicotinic antagonists
Parasiticides
Permeation enhancers
Stomach
Vasodilators
(enhancement of bioavailability of peptides with bile salts)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

IT Antibodies
Blood-coagulation factors
Ferritins
Glycoproteins, general, biological studies
Hemoglobins
Interferons
Oligonucleotides
Opioids
Polynucleotides
Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

IT Bile salts
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

IT Gastrointestinal motility
(gastric, drugs for treatment of; enhancement of bioavailability of

peptides with bile salts)
IT Drug delivery systems
(oral; enhancement of bioavailability of peptides with bile salts)
IT Drug delivery systems
(parenterals; enhancement of bioavailability of peptides with bile salts)
IT Antiulcer agents
(peptic; enhancement of bioavailability of peptides with bile salts)
IT Neuropeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmitters; enhancement of bioavailability of peptides with bile salts)
IT 9001-08-5D, inhibitor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticholinesterase; enhancement of bioavailability of peptides with bile salts)
IT 50-56-6, Oxytocin, biological studies 1393-25-5, Secretin 8001-27-2, Hirudin 9001-05-2, Catalase 9001-27-8, Factor viii 9001-28-9, Factor IX 9002-60-2, Acth, biological studies 9002-61-3, Chorionic gonadotropin 9002-64-6, Parathyroid hormone 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone 9002-71-5, Thyroid stimulating hormone 9002-72-6, Somatotropin 9002-76-0, Gastrin 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-43-6, Cytochrome c, biological studies 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-71-8, Corticotropin releasing hormone 9015-94-5, Renin, biological studies 9034-39-3, Growth hormone releasing hormone 9034-40-6, Gonadotropin releasing hormone 9038-70-4, Somatomedin 9039-53-6, Urokinase 9041-90-1, Angiotensin I 9054-89-1, Superoxide dismutase 9087-70-1, Aprotinin 11000-17-2, Antidiuretic hormone 11096-26-7, Erythropoietin 11128-99-7, Angiotensin II 24305-27-9, Thyrotropin releasing hormone 51110-01-1, Somatostatin 57285-09-3, Inhibin 59392-49-3, Gastric inhibitory peptide 67763-96-6, Igf1 67763-97-7, Igf2 80043-53-4, Gastrinreleasing peptide 85637-73-6, Atrial natriuretic hormone 89750-14-1, Glucagon-like peptide I 119418-04-1, Galanin 139639-23-9, Tissue plasminogen activator
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)
IT 79-14-1D, Glycolic acid, salts 81-24-3D, Taurocholic acid, salts 81-25-4, Cholic acid 83-44-3D, Deoxycholic acid, salts 128-13-2D, Ursodeoxycholic acid, salts 360-65-6D, Glycodeoxycholic acid, salts 474-25-9D, Chenodeoxycholic acid, salts 474-74-8D, Glycolithocholic acid, salts 516-35-8D, Taurochenodeoxycholic acid, salts 516-50-7D, Taurodeoxycholic acid, salts 516-90-5D, TAurolithocholic acid, salts 640-79-9D, Glycochenodeoxycholic acid, salts 14605-22-2D, Tauroursodeoxycholic acid, salts 63948-32-3 64480-66-6D, Glycoursodeoxycholic acid, salts 83381-47-9, Gastrin-34 I (rat) 171511-54-9 324753-46-0 325142-35-6
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)
IT 9003-99-0, Peroxidase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(horseradish; enhancement of bioavailability of peptides with bile salts)
IT 9002-10-2, Tyrosinase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mushroom; enhancement of bioavailability of peptides with bile salts)

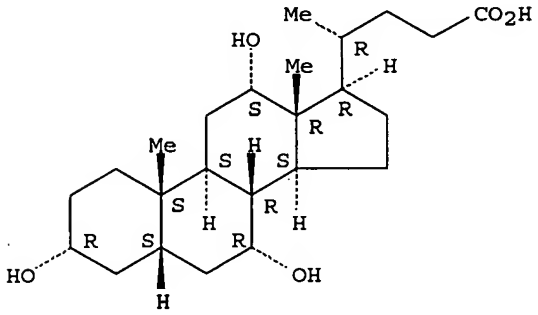
IT 9035-81-8, Trypsin inhibitor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soy bean; enhancement of bioavailability of peptides with bile salts)

IT 81-25-4, Cholic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhancement of bioavailability of peptides with bile salts)

RN 81-25-4 HCAPLUS

CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L30 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1991:580392 HCAPLUS

DN 115:180392

ED Entered STN: 01 Nov 1991

TI The effect of sodium deoxycholate and other surfactants on the mucosal surface pH in proximal jejunum of rat

AU McKie, A. T.; Stewart, W.; Lucas, M. L.

CS Inst. Physiol., Glasgow Univ., Glasgow, G12 8QQ, UK

SO Naunyn-Schmiedeberg's Archives of Pharmacology (1991), 343(6), 659-64
CODEN: NSAPCC; ISSN: 0028-1298

DT Journal

LA English

CC 13-7 (Mammalian Biochemistry)

AB The mucosal surface pH (acid microclimate) and nucleotide levels of rat proximal jejunum were measured in vivo under various conditions which included exposure to pharmacol. agents and to surfactants. Mucosal surface pH was unaffected by sodium nitroprusside, A 23187, and amiloride, as was mucosal cGMP content, although amiloride and A 23187 reduced cAMP content. In contrast, surfactants elevated the pH of the mucosal surface significantly: control value 6.23; Lubrol PX 0.8% (volume/volume) 6.98 sodium deoxycholate 2 mM 6.67; Triton X 100 0.5% (volume/volume) 7.41. No significant changes in cGMP levels were noted after surfactant treatment, although deoxycholate and Triton X 100 reduced cAMP levels. The ability of higher concns. of surfactant to elevate the mucosal surface pH beyond neutrality to values similar to plasma pH contrasts with the action of Escherichia coli heat-stable (STa) enterotoxin, which at high concns. could not elevate the mucosal surface pH beyond neutrality. Consistent with the known effects on tight junction permeability, surfactants may act by allowing plasma-like subepithelial fluid to neutralize the microclimate.

ST jejunum mucosa pH surfactant; cAMP jejunum mucosa pH surfactant; cGMP jejunum mucosa pH surfactant

IT Surfactants

(proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)

IT Intestine
(jejunum, proximal, mucosa, surface pH of, surfactants effect on, ion movements and cyclic nucleotides in relation to)

IT 7440-23-5, Sodium, biological studies
RL: BIOL (Biological study)
(hydrogen ion exchange with, in jejunum mucosa, effect of surfactant on surface pH in relation to)

IT 60-92-4, CAMP 7665-99-8, CGMP
RL: BIOL (Biological study)
(of jejunum mucosa, surfactants effect on, mucosal surface pH in relation to)

IT **302-95-4**, Sodium deoxycholate 577-11-7 9002-92-0, Lubrol PX
9002-93-1, Triton X-100
RL: BIOL (Biological study)
(proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)

IT 12408-02-5, Hydrogen ion, biological studies
RL: BIOL (Biological study)
(sodium exchange with, in jejunum mucosa, effect of surfactant on surface pH in relation to)

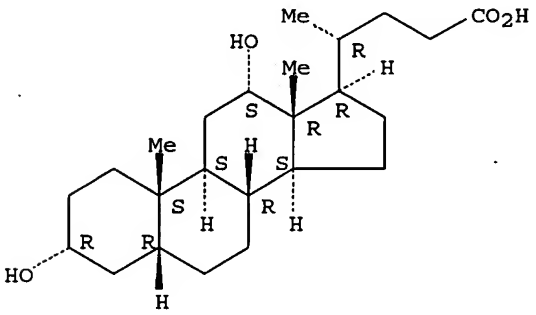
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(transport of, by jejunum mucosa, surfactants effect on surface pH and cyclic nucleotides in relation to)

IT **302-95-4**, Sodium deoxycholate
RL: BIOL (Biological study)
(proximal jejunum mucosal surface pH response to, ion movements and cyclic nucleotides in relation to)

RN 302-95-4 HCAPLUS

CN Cholan-24-oic acid, 3,12-dihydroxy-, monosodium salt, (3α,5β,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

L30 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1984:32553 HCAPLUS

DN 100:32553

ED Entered STN: 12 May 1984

TI The effect of deoxycholate on intestinal surface pH and 5-methyltetrahydropteroylglutamate absorption in the rat proximal jejunum in vitro

AU Blair, John A.; Hilburn, Michael E.; **Lucas, Michael L.**; Said, Hamid M.

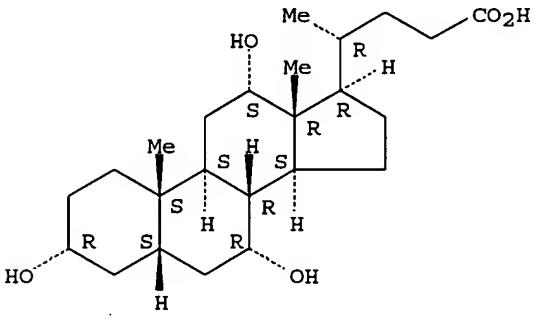
CS Dep. Chem., Univ. Aston, Birmingham, B4 7ET, UK

SO Biochemical Society Transactions (1983), 11(2), 165-7

Search done by Noble Jarrell

CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English
CC 13-2 (Mammalian Biochemistry)
AB The effects of deoxycholate (0.01-10 mM) on rat proximal jejunum in vitro indicated that intestinal surface pH is a determinant of folate absorption.
ST intestine pH folate absorption deoxycholate
IT Bile acids
RL: BIOL (Biological study)
(folate absorption by intestinal jejunum response to, surface pH in relation to)
IT Intestine, metabolism
(proximal jejunum, folate absorption by, deoxycholate effect on, surface pH in relation to)
IT 59-30-3, biological studies 134-35-0
RL: BIOL (Biological study)
(absorption of, by proximal jejunum, deoxycholate effect on, surface pH in relation to)
IT 81-25-4 360-65-6
RL: BIOL (Biological study)
(folate absorption by intestinal jejunum response to, surface pH in relation to)
IT 83-44-3
RL: BIOL (Biological study)
(folate absorption by proximal jejunum response to, surface pH in relation to)
IT 81-25-4
RL: BIOL (Biological study)
(folate absorption by intestinal jejunum response to, surface pH in relation to)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alph
a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d all hitstr l40 tot

L40 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:537280 HCAPLUS
DN 138:85395
ED Entered STN: 19 Jul 2002
TI Participation of two members of the very long-chain acyl-CoA synthetase family in bile acid synthesis and recycling
AU Mihalik, Stephanie J.; Steinberg, Steven J.; Pei, Zhengtong; Park, Joseph; Kim, Do G.; Heinzer, Ann K.; Dacremont, Georges; Wanders, Ronald J. A.; Cuebas, Dean A.; Smith, Kirby D.; Watkins, Paul A.
CS Kennedy Krieger Institute and the Department of Pediatrics, Johns Hopkins

University School of Medicine, Baltimore, MD, 21205, USA
SO Journal of Biological Chemistry (2002), 277(27), 24771-24779
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-2 (Enzymes)
Section cross-reference(s): 3, 13
OS CASREACT 138:85395
AB Bile acids are synthesized de novo in the liver from cholesterol and conjugated to glycine or taurine via a complex series of reactions involving multiple organelles. Bile acids secreted into the small intestine are efficiently reabsorbed and reutilized. Activation by thioesterification to CoA is required at two points in bile acid metabolism First, 3α,7α,12α-trihydroxy-5β-cholestanoic acid, the 27-carbon precursor of cholic acid, must be activated to its CoA. derivative before side chain cleavage via peroxisomal β-oxidation Second, reutilization of cholate and other C24 bile acids requires reactivation prior to re-conjugation. We reported previously that homolog 2 of very long-chain acyl-CoA synthetase (VLCS) can activate cholate. We now show that homolog 2 also activates chenodeoxycholate, the secondary bile acids deoxycholate and lithocholate, and 3α,7α,12α-trihydroxy-5β-cholestanoic acid. In contrast, VLCS activated 3α,7α,12α-trihydroxy-5β-cholestanoate, but did not utilize any of the C24 bile acids as substrates. We hypothesize that the primary function of homolog 2 is in the reactivation and recycling of C24 bile acids, whereas VLCS participates in the de novo synthesis pathway. Results of in situ hybridization, topog. orientation, and inhibition studies are consistent with the proposed roles of these enzymes in bile acid metabolism
ST very long chain acyl CoA synthetase bile acid recycling; mouse cDNA sequence bile acid CoA synthetase liver
IT Mus musculus
(VLCS cDNA sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT Liver
(hepatocyte, compartmentalized expression of VLCS; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT Molecular topology
(membrane topol. of VLCS-H2; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT Protein sequences
cDNA sequences
(of VLCS of mouse liver; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 114797-03-4P, Bile acid-CoA synthetase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(VLCS homolog 2; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

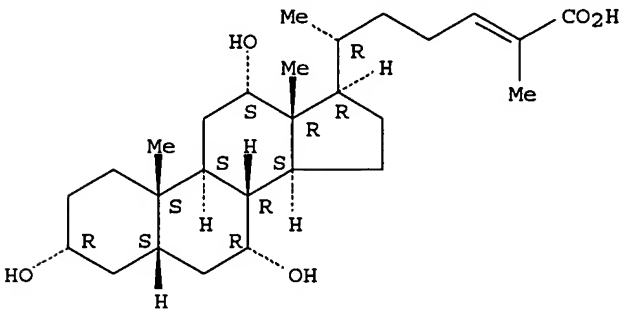
IT 69403-06-1P, Very long-chain acyl-CoA synthetase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(VLCS; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 470737-50-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 83-44-3, Deoxycholic acid 434-13-9, Lithocholic acid 474-25-9, Chenodeoxycholic acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 547-98-8P
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(enzyme substrate specificity; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 5226-26-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation of bile acid precursor THCA; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 3396-82-5, Sodium cyanide (Na(14CN))
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation of 14C-labeled trihydroxycholestanate; bile acid-CoA synthetase activity and cellular localization of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 114416-41-0P 114443-04-8P 114443-05-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation of 14C-labeled trihydroxycholestanate; bile acid-CoA synthetase activity and cellular localization of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 200385-45-1, GenBank AF033031
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
IT 114416-40-9P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(14C-labeled enzyme substrate; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Antonenkov, V; J Biol Chem 1997, V272, P26023 HCAPLUS
(2) Bahar, R; Gastroenterol Clin North Am 1999, V28, P27 MEDLINE
(3) Carey, M; The Liver:Biology and Pathobiology, 3rd Ed 1994, P719

(4) Dieuaide-Noubhani, M; Eur J Biochem 1996, V240, P660 HCAPLUS
(5) Giger, R; J Comp Neurol 1996, V375, P378 HCAPLUS
(6) Hofmann, A; The Liver:Biology and Pathobiology, 3rd Ed 1994, P677
(7) Kase, B; J Biol Chem 1989, V264, P9220 HCAPLUS
(8) Kase, F; J Lipid Res 1983, V24, P1560 HCAPLUS
(9) Katz, N; Eur J Biochem 1983, V135, P103 HCAPLUS
(10) Katz, N; Eur J Biochem 1989, V180, P185 HCAPLUS
(11) Killenberg, P; J Lipid Res 1978, V19, P24 HCAPLUS
(12) Kurosawa, T; Anal Chim Acta 1998, V365, P249 HCAPLUS
(13) Lim, W; Biochem J 1981, V197, P611 HCAPLUS
(14) Lowry, O; J Biol Chem 1951, V193, P265 HCAPLUS
(15) Polokoff, M; J Biol Chem 1977, V252, P1167 HCAPLUS
(16) Rost, B; Protein Sci 1995, V4, P521 HCAPLUS
(17) Schepers, L; Biochem J 1989, V257, P221 HCAPLUS
(18) Setchell, K; Liver Disease in Children, 2nd Ed 2001, P701
(19) Smith, B; Exp Cell Res 2000, V254, P309 HCAPLUS
(20) Solaas, K; J Lipid Res 2000, V41, P1154 HCAPLUS
(21) Steinberg, S; Ann Neurol 1999, V46, P409 HCAPLUS
(22) Steinberg, S; Biochem Biophys Res Commun 1999, V257, P615 HCAPLUS
(23) Steinberg, S; J Biol Chem 2000, V275, P15605 HCAPLUS
(24) Steinberg, S; Mol Genet Metab 1999, V68, P32 HCAPLUS
(25) Tserng, K; J Lipid Res 1977, V18, P400 HCAPLUS
(26) Twisk, J; J Clin Invest 1995, V95, P1235 HCAPLUS
(27) Uchiyama, A; J Biol Chem 1996, V271, P30360 HCAPLUS
(28) van Grunsven, E; Proc Natl Acad Sci U S A 1998, V95, P2128 HCAPLUS
(29) van Veldhoven, P; J Biol Chem 1992, V267, P20065 HCAPLUS
(30) Vanhove, G; J Biol Chem 1993, V268, P10335 HCAPLUS
(31) Vlahcevic, Z; Gastroenterol Clin North Am 1999, V28, P1 MEDLINE
(32) Wanders, R; The Metabolic & Molecular Bases of Inherited Disease, 8th Ed 2001, P3219
(33) Watkins, P; Am J Hum Genet 1995, V57, P292 HCAPLUS
(34) Wheeler, J; Arch Biochem Biophys 1997, V348, P15 HCAPLUS
(35) Xu, R; Biochem Biophys Res Commun 1996, V221, P271 HCAPLUS

IT 5226-26-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation of bile acid precursor THCA; bile acid-CoA synthetase activity, cellular localization, and membrane topog. of two very long-chain acyl-CoA synthetase (VLCS) family proteins suggests a role in bile acid synthesis and recycling)

RN 5226-26-6 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L40 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:508917 HCAPLUS
DN 133:140227
ED Entered STN: 27 Jul 2000
TI Method and compositions for lipidization of hydrophilic molecules

IN Shen, Wei-chiang; Wang, Jinghua
PA The University of Southern California, USA
SO U.S., 34 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-28
INCL 514003000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6093692	A	20000725	US 1997-936898	19970925 <--
PRAI US 1996-77177P	P	19960926 <--		
US 1997-49499P	P	19970613 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6093692	ICM	A61K038-28
	INCL	514003000
US 6093692	NCL	514/003.000; 514/002.000; 514/009.000; 514/019.000; 514/023.000; 530/300.000; 530/303.000; 530/307.000; 530/315.000; 530/317.000; 530/331.000; 530/333.000; 530/350.000
	ECLA	A61K047/48H4 <--

OS MARPAT 133:140227
AB Fatty acid derivs. of disulfide-containing compds. (for example, disulfide-containing peptides or proteins) comprising fatty acid-**conjugated** products with a disulfide linkage are employed for delivery of the compds. to mammalian cells. This modification markedly increases the absorption of the compds. by mammalian cells relative to the rate of absorption of the **unconjugated** compds., as well as prolonging blood and tissue retention of the compds. Moreover, the disulfide linkage in the **conjugate** is quite labile in vivo and thus facilitates intracellular or extracellular release of the intact compds. from the fatty acid moieties. N-palmityl-2-pyridyldithiocysteine was prepared and reacted with Bowman-Birk inhibitor (BBI) to obtain a palmityl disulfide **conjugate** of BBI. When the **conjugate** was incubated with colon carcinoma cells (Caco-2) in serum-free medium, the uptake of the **conjugate** was higher than that of BBI.
ST fatty acid disulfide protein **conjugate** bioavailability
IT Antisense oligonucleotides
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(complementary to mRNA of monoamine oxidase B, palmitylated; **conjugates** of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
IT Drug bioavailability
Drug delivery systems
(**conjugates** of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
IT Amino acids, biological studies
Carbohydrates, biological studies
Nucleosides, biological studies
Nucleotides, biological studies
Oligonucleotides
Peptides, biological studies
Proteins, general, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** with fatty acid disulfide derivs.; **conjugates** of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
IT Fatty acids, biological studies
Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(disulfide derivs., conjugates with proteins; conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT Biological transport
(drug; conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT Drug delivery systems
(liposomes; conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 16679-58-6DP, Desmopressin, fatty acid disulfide conjugates 37330-34-0DP, Bowman-Birk inhibitor, oleyl disulfide conjugate 37330-34-0DP, Bowman-Birk inhibitor, reaction product with N-succinimidyl-3-(2-pyridyidithio)propionate and N-Palmityl-2-pyridyldithiocysteine 171735-25-4DP, reaction products with proteins 254453-83-3P 286365-28-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 285981-92-2P 285981-94-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 57-11-4D, Stearic acid, disulfide derivs., conjugates with proteins 81-25-4D, disulfide derivs., conjugates with proteins 83-44-3D, disulfide derivs., conjugates with proteins 112-80-1D, Oleic acid, disulfide derivs., conjugates with proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 9003-99-0DP, Peroxidase, reaction product with N-succinimidyl-3-(2-pyridyidithio)propionate and N-Palmityl-2-pyridyldithiocysteine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(horseradish; conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 9003-99-0, Peroxidase
RL: RCT (Reactant); RACT (Reactant or reagent)
(horseradish; preparation of conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 52-90-4, L-Cysteine, reactions 83-44-3 1200-22-2, Lipoic acid 2127-03-9, 2,2'-Dithiobis(pyridine) 6066-82-6, N-Hydroxysuccinimide 14464-31-4 16679-58-6, Desmopressin 37330-34-0, Bowman-Birk inhibitor 47931-85-1, Salmon calcitonin 59277-89-3, Acyclovir 68181-17-9, SPDP
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

IT 25596-79-6P, Calcitonin (salmon reduced) 37330-34-0DP, Bowman-Birk inhibitor, reaction product with N-succinimidyl-3-(2-pyridyidithio)propionate 88442-68-6P 119364-41-9P 171735-25-4P 174069-00-2P 177902-84-0P 285981-91-1P 285981-93-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; J Pharm Sci 1990, V79(7), P595
(2) Broadwell, R; Proc Natl Acad Sci USA 1988, V85(2), P632 HCAPLUS
(3) Brocklehurst, K; Biochem J 1973, V135(1), P573
(4) Chekhonin, V; FEBS Letters 1991, V287(1,2), P149

(5) Chu, Y; Biochem 1994, V33(44), P13087 HCAPLUS
(6) Conradi, R; Pharm Res 1991, V8(12), P1453 HCAPLUS
(7) Edwards, P; British Med Bulletin 1978, V34(1), P55 HCAPLUS
(8) Ekrami, H; A Dissertation, UMI Dissertation Services, Chapter 11 1995, P98
(9) Ekrami, H; FEBS Letters 1995, V371(3), P283 HCAPLUS
(10) Eriksson, S; Biochim Biophys Acta E 1970, V212(3), P518 HCAPLUS
(11) Eriksson, S; Chem Abstracts 1970, P25 HCAPLUS
(12) Fix, J; Amer J Physiology 1986, V251(3, Prt 1), PG332
(13) Friden, P; Frontiers In Cerebral Vascular Biology, Transport and Its Regulation 1993, P129 HCAPLUS
(14) Gonzalez-Mariscal, L; J Membrane Biol 1985, V86(2), P113 HCAPLUS
(15) Gordon, G; Proc Natl Acad Sci USA 1985, V82(21), P7419 HCAPLUS
(16) Hashimoto, M; Pharm Res 1989, V6(2), P171 HCAPLUS
(17) Huang, W; Mol Immunol 1994, V31(15), P1191 HCAPLUS
(18) Hughes, R; J Pharm Sci 1991, V80(12), P1103 HCAPLUS
(19) Hughes, R; J Pharm Sci 1992, V81(8), P845 HCAPLUS
(20) Inagaki, M; Rhinology 1985, V23(3), P213 MEDLINE
(21) Kabanov, A; Protein Engineering 1989, V3(1), P39 HCAPLUS
(22) Kajii, H; Life Science 1985, V37(6), P523 HCAPLUS
(23) Kauvar; US 5599903 1997 HCAPLUS
(24) Kauvar; US 5679643 1997 HCAPLUS
(25) Kauvar; US 5763570 1998 HCAPLUS
(26) Kidron, M; Life Sci 1982, V31(25), P2837 HCAPLUS
(27) Landolph, J; Transformation Assay of Established Cell Lines:Mechanisms and Application 1985, V67, P185 HCAPLUS
(28) Lee, V; Crit Rev Ther Drug Carrier Syst 1988, V5(2), P69 HCAPLUS
(29) Lee, V; Crit Rev Ther Drug Carrier Syst 1991, V8(2), P91 HCAPLUS
(30) Leone-Bay; US 5629020 1997 HCAPLUS
(31) Letsinger, R; Proc Natl Acad Sci 1989, V80(17), P6553
(32) Lowry, O; J Biol Chem 1951, V193, P265 HCAPLUS
(33) Martins, M; Biochimie 1990, V72(9), P671 HCAPLUS
(34) McConahey, P; Methods Enzymol 1980, V70(A), P210 MEDLINE
(35) Mostov, K; Cell 1985, V43(2), P389 HCAPLUS
(36) Muller, C; International J Pharmaceutics 1989, V57, P41
(37) Muranishi, S; Pharm Res 1991, V8(5), P649 HCAPLUS
(38) Naftilan; US 5635380 1997 HCAPLUS
(39) Reznikoff, C; Cancer Res 1973, V33(12), P3231 MEDLINE
(40) Reznikoff, C; Cancer Res 1973, V33(12), P3239 HCAPLUS
(41) Sett, R; J Infectious Dis 1993, V168(4), P994 HCAPLUS
(42) Shen, W; Adv Drug Delivery Rev 1992, V8(1), P93 HCAPLUS
(43) Shen, W; Proc Natl Acad Sci USA 1981, V78(12), P7589 HCAPLUS
(44) Smith, P; Adv Drug Delivery Rev 1992, V8(2,3), P253
(45) Stn Information Service; File Registry
(46) Takaori, K; Biochem Biophys Res Commun 1986, V137(2), P682 HCAPLUS
(47) Taub, M; J Cell Phys 1992, V150(2), P283 HCAPLUS
(48) Toth, I; J Drug Targeting 1994, V2(3), P217 HCAPLUS
(49) Ubuka, T; "Synthesis of disulfides related to glutathione and their detection in tissue,", Abstract No 156843v 1987 HCAPLUS
(50) Ubuka, T; (Ganryu Aminosan) Sulfur Amino Acids 1985, V8(1), P153 HCAPLUS
(51) Uchimi, I; "Glutathione derivatives,", Abstract No 54179m 1971 HCAPLUS
(52) Uchimi, I; "Glutathione derivatives,", Abstract No 56440t 1970 HCAPLUS
(53) Vetvicka, V; Crit Rev Ther Drug Carrier Syst 1988, V5(3), P141 HCAPLUS
(54) Vitetta, E; J Clin Immunol 1990, V10(6 Suppl), P15S MEDLINE
(55) Wan, J; J Biol Chem 1992, V267(19), P13446 HCAPLUS
(56) Wan, J; J Cell Phys 1990, V145(1), P9 HCAPLUS
(57) Wan, J; Pharm Res 1991, V8(10 Suppl), PS
(58) Willner; US 5708146 1998 HCAPLUS
(59) Yavelow, J; Cancer Res 1983, V43(5 Suppl), P2454s MEDLINE
(60) Yodoya, E; J Pharm Ex Ther 1994, V271(3), P1509 HCAPLUS
(61) Yoshikawa, H; Pharm Res 1985, V5, P249

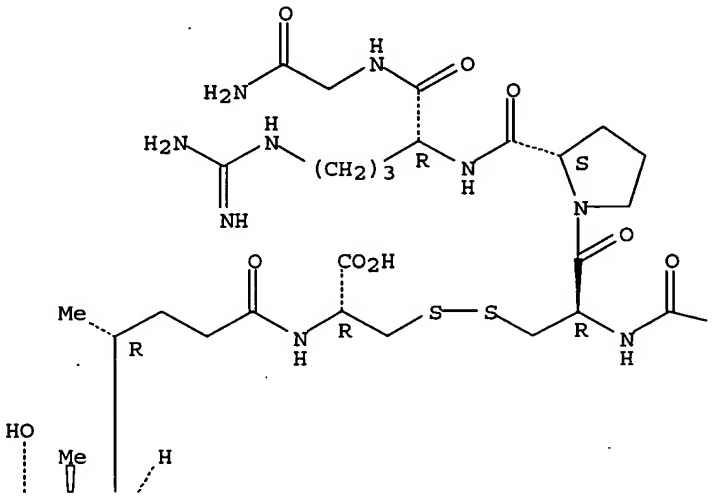
IT **285981-92-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)

RN 285981-92-2 HCAPLUS

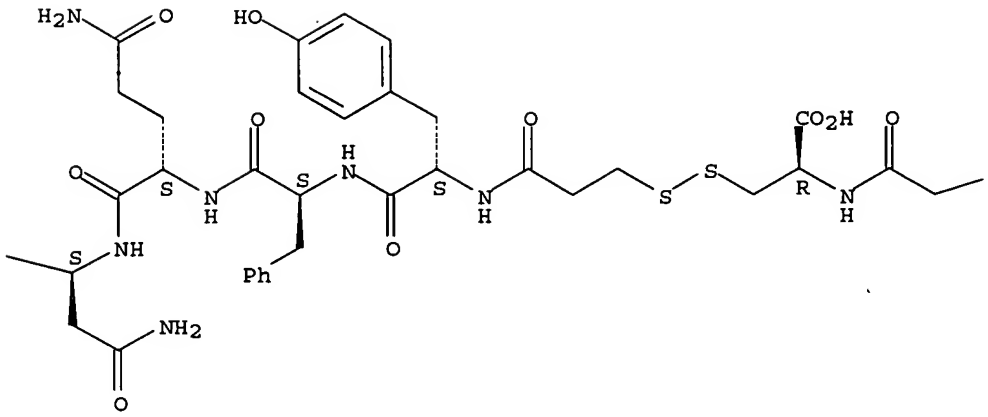
CN Glycinamide, N-(3-mercapto-1-oxopropyl)-L-tyrosyl-L-phenylalanyl-L-glutaminyl-L-asparaginyl-L-cysteinyl-L-prolyl-D-arginyl-, bis(disulfide) with N-[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]-L-cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

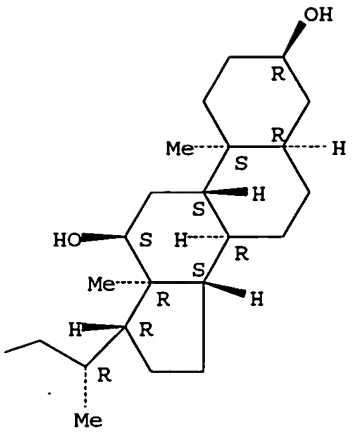
PAGE 1-A



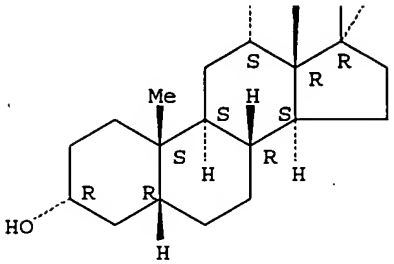
PAGE 1-B



PAGE 1-C

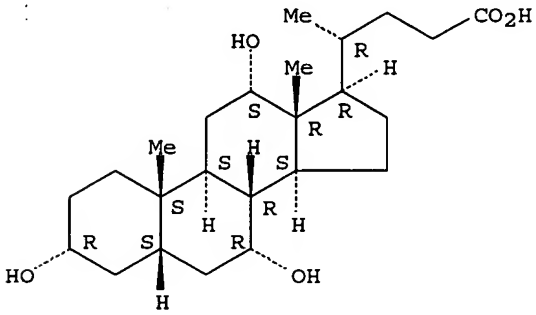


PAGE 2-A



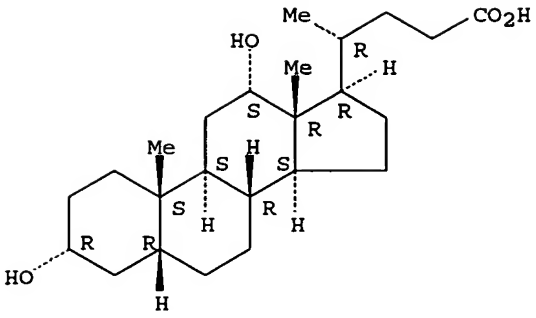
IT 81-25-4D, disulfide derivs., conjugates with proteins
83-44-3D, disulfide derivs., conjugates with proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



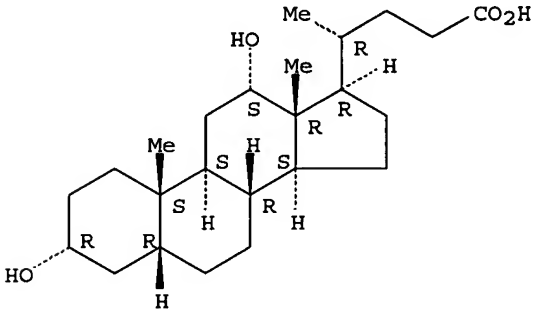
RN 83-44-3 HCAPLUS
CN Cholan-24-oic acid, 3,12-dihydroxy-, (3α,5β,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



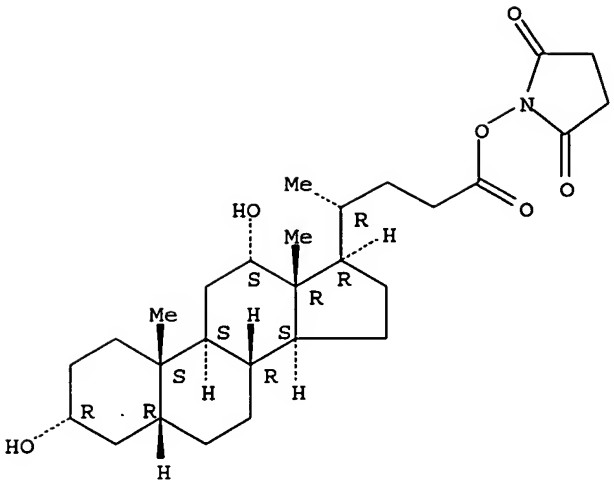
IT 83-44-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
RN 83-44-3 HCAPLUS
CN Cholan-24-oic acid, 3,12-dihydroxy-, (3α,5β,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



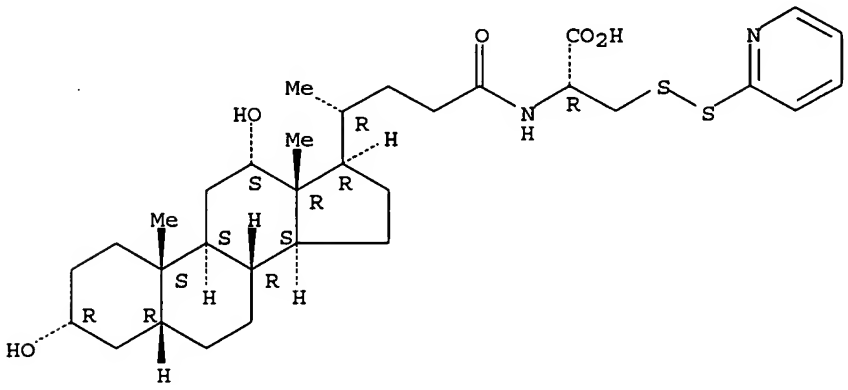
IT 174069-00-2P 285981-91-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of conjugates of hydrophilic mols. with fatty acid or steroid disulfide derivs. for improving their bioavailabilities)
RN 174069-00-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 285981-91-1 HCAPLUS
CN L-Alanine, N-[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]-3-(2-pyridinyldithio)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2000:10612** HCAPLUS
DN 132:73648
ED Entered STN: 06 Jan 2000
TI Lipophilic insulin derivatives soluble at physiological pH with prolonged serum half-lives and biological activity
IN Havelund, Svend; Halstrom, John; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan
PA Novo Nordisk A/S, Den.
SO U.S., 47 pp., Cont.-in-part of U.S. 5,750,497.
CODEN: USXXAM
DT Patent
LA English
IC C07K014-62; A61K038-28
INCL 514003000
CC 1-10 (Pharmacology)
Section cross-reference(s): 2
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 6011007	A	20000104	US 1997-975365	19971120 <--
	ZA 9407187	A	19950317	ZA 1994-7187	19940916 <--
	JP 2000060556	A2	20000229	JP 1999-221632	19940916 <--
	EP 1132404	A2	20010912	EP 2001-112992	19940916 <--
	EP 1132404	A3	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT				
	JP 2002308899	A2	20021023	JP 2001-385921	19940916 <--
	US 5750497	A	19980512	US 1995-400256	19950308 <--
	US 6869930	B1	20050322	US 1999-398365	19990917 <--
	AU 745983	B2	20020411	AU 2000-51960	20000811 <--
	US 2004110664	A1	20040610	US 2002-101454	20020312 <--
PRAI	DK 1993-1044	A	19930917 <--		
	US 1995-400256	A2	19950308 <--		
	US 1994-190829	A	19940202 <--		
	EP 1994-926816	A3	19940916 <--		
	JP 1995-508923	A3	19940916 <--		
	JP 1999-221632	A3	19940916 <--		
	US 1997-975365	A3	19971120 <--		
	US 1999-398365	A1	19990917 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
US 6011007	IC	C07K014-62IC A61K038-28	
	INCL	514003000	
US 6011007	NCL	514/003.000; 514/866.000; 530/303.000; 530/304.000	
	ECLA	C07K014/62	<--
EP 1132404	ECLA	C07K014/62	<--
US 5750497	NCL	514/003.000; 514/866.000; 530/304.000	
	ECLA	C07K014/62	<--
US 6869930	NCL	514/003.000; 514/866.000; 530/304.000	
	ECLA	C07K014/62	<--
US 2004110664	NCL	514/003.000	
	ECLA	C07K014/62	<--

OS MARPAT 132:73648

AB Human insulin derivs. with improved solubility at physiol. pH and that retain biol. activity for longer than wild-type human insulin are described. The insulins are substituted at positions A21 and B3 with either being any amino acid except lysine, arginine, or cysteine. The phenylalanine at B1 may be deleted and the amino acid at position B30 may be deleted or substituted by any amino acid except lysine, arginine, or cysteine or by another amino acid that is lipophilic having a C10-24 side chain. If B30 is deleted or substituted, lysineB29 is modified by a carboxylic acid connected to the ε-amino group. When B30 is threonine or alanine and A21 and B3 are both asparagine, and phenylalanineB1 is present, then the insulin derivative is always present as a Zn2 complex.

ST human insulin sequence acylation diabetes pharmaceutical; lipophilic insulin deriv antidiabetic

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(C5, insulins modified with; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Solubility
(at physiol. pH; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dicarboxylic, C<6, insulin modification by; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT cDNA sequences
(for insulin analogs of human; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT **Drug delivery systems**
(injections, insulin; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Antidiabetic agents

(insulin analogs as; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Acetyl group
Formyl group
(insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Fatty acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Protein sequences
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Lipophilicity
(of insulin derivs.; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Plasmids
(pAK-series and pKFN1627 and pEA-series; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT Functional groups
(propionyl, insulin derivs. containing; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 14464-31-4 69888-86-4 88404-23-3 104943-24-0 165893-02-7
165893-03-8 **168986-19-4** 168986-20-7 169142-69-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of insulin derivs. using; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 169148-55-4DP, zinc complexes 169148-56-5DP, zinc complexes
169148-57-6P 169148-58-7P 169148-59-8P 169148-60-1P 169148-61-2DP,
zinc complexes 169148-62-3DP, zinc complexes 169148-63-4P
169148-64-5P 169148-65-6P 169148-66-7P 169148-67-8P 169148-68-9P
169148-69-0P 169148-70-3P 169148-71-4P 169148-72-5DP, zinc complexes
169148-73-6P 169148-74-7DP, zinc complexes 169148-75-8DP, zinc
complexes 169535-16-4P 169535-18-6P 169535-20-0P 169535-22-2P
169535-24-4P 169535-26-6P 169535-28-8P 169535-30-2P 169535-32-4P
169535-34-6P 169535-36-8P 169535-38-0P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 11061-68-0D, Insulin (human), amino acid-substituted, derivatized
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

IT 51-49-0DP, **conjugates** with insulin 108-30-5DP,
conjugates with insulin 110-15-6DP, Butanedioic acid,
conjugates with insulin, preparation 143-07-7DP, Dodecanoic
acid, **conjugates** with insulin, preparation 544-63-8DP,
Tetradecanoic acid, **conjugates** with insulin, preparation
638-53-9DP, Tridecanoic acid, **conjugates** with insulin
7145-63-3DP, **conjugates** with insulin 7452-59-7DP,
conjugates with insulin 7769-79-1DP, **conjugates** with
insulin 14565-47-0DP, **conjugates** with insulin 17702-88-4DP,
conjugates with insulin 22102-66-5DP, **conjugates** with
insulin 35237-37-7DP, **conjugates** with insulin 68528-80-3DP,
conjugates with insulin **104211-94-1DP**,
conjugates with insulin 141537-81-7DP, **conjugates** with
insulin 158627-30-6DP, **conjugates** with insulin
168986-14-9DP, **conjugates** with insulin 168986-15-0DP,
conjugates with insulin 168986-16-1DP, **conjugates** with
insulin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum

half-lives and biol. activity)
IT 23713-49-7DP, Zinc dication, complexes with insulin derivs., biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
IT 169535-21-1P 169535-23-3P, DNA (Saccharomyces cerevisiae synthetic signal peptide LaC212spx3 fusion protein with synthetic peptide fusion protein with human insulin A chain [21-glycine] fusion protein with human insulin B-chain [3-aspartic acid]-specifying cDNA plus flanks)
169535-27-7P 169535-29-9P 169535-33-5P 169535-35-7P 169535-37-9P
169535-39-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
IT 169535-17-5, DNA (Saccharomyces cerevisiae clone pAK188 synthetic signal peptide LaC212spx3 fusion protein with human clone pAK188 1-29-insulin B-chain fusion protein with synthetic clone pAK188 5-amino acid peptide fusion protein with human clone pAK188 insulin A-chain-specifying plus flanks) 169535-19-7 169535-25-5, DNA (Saccharomyces cerevisiae synthetic signal peptide LaC212spx3 fusion protein with human insulin A-chain [21-glycine] fusion protein with human insulin B-chain [3-aspartic acid]-specifying cDNA plus flanks)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
IT 24424-99-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(protecting group; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
IT 222586-86-9, 3: PN: US6011007 SEQID: 3 unclaimed DNA 222586-87-0, 4: PN: US6011007 SEQID: 4 unclaimed DNA 222586-88-1, 5: PN: US6011007 SEQID: 5 unclaimed DNA 222586-89-2, 6: PN: US6011007 SEQID: 6 unclaimed DNA
222586-90-5, 7: PN: US6011007 SEQID: 7 unclaimed DNA 222586-91-6, 8: PN: US6011007 SEQID: 8 unclaimed DNA 222586-92-7, 9: PN: US6011007 SEQID: 9 unclaimed DNA 222586-93-8 222586-94-9 222586-95-0 222586-96-1
222586-98-3 222587-00-0 222587-09-9
RL: PRP (Properties)
(unclaimed nucleotide sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
IT 253597-47-6 253597-48-7
RL: PRP (Properties)
(unclaimed protein sequence; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; GB 1492997 1977 HCAPLUS
(2) Anon; JP 5767548 1982
(3) Anon; WO 9112817 1991 HCAPLUS
(4) Anon; Prescription Products Guide 1992, P942
(5) Brange And Langkjaer; Chemical Stability of Insulin Acta Pharm Nord 1992, V4(3), P149
(6) Breddam; US 4645740 1987 HCAPLUS
(7) Doerge; Wilson and Gisvold's textbook of organic medicinal and pharmaceutical chemistry 1982, P774
(8) Foye, W; Principles of Medicinal Chemistry 1974, P563
(9) Gammelhoft; Phys Rev 1984, V64, P1321
(10) Grant; US 3823125 1974 HCAPLUS
(11) Haas; US 3528960 1970 HCAPLUS
(12) Kurtz; Diabetologia 1983, V25, P322 MEDLINE
(13) Lindsay; US 3950517 1976 HCAPLUS
(14) Lindsay And Shall; The Acetylation of Insulin Biochem 1991, V121, P737

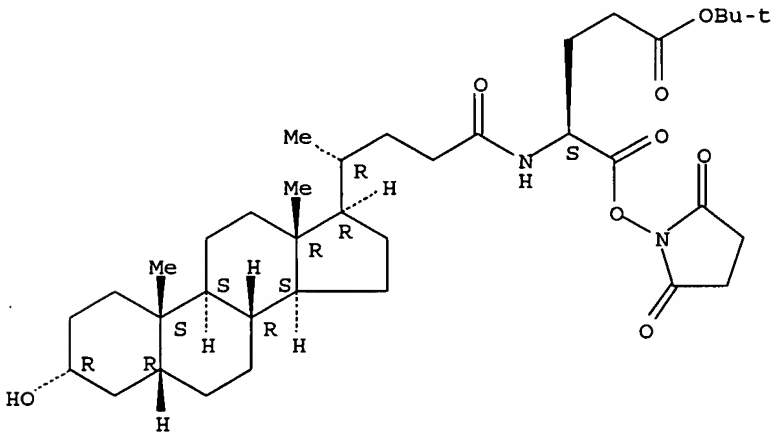
(15) Marble, A; Joslin's Diabetes Mellitus, 12th Edition 1985, P380
(16) Markussen; US 5008241 1991 HCAPLUS
(17) Markussen; Prot Eng 1987, V1, P205 HCAPLUS
(18) Markussen; Prot Eng 1988, V2, P157 HCAPLUS
(19) Mims Annual; Section 6d "Insulin Preparations" 1991
(20) Mims Annual; Section 6d "Insulin Preparations" 1993
(21) Panayotis; US 5208217 1993 HCAPLUS
(22) Samuel; Clin Exp Immunol 1978, V33, P252 HCAPLUS
(23) Schade; Exerpta Medica 1983, P7
(24) Schlichtkrull, J; "Insulin Crystals" (Ejnar Munksgaard) 1958, P21
(25) Smyth; US 3868356 1975 HCAPLUS

IT 168986-19-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of insulin derivs. using; lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

RN 168986-19-4 HCAPLUS

CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[(3α,5β)-3-hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

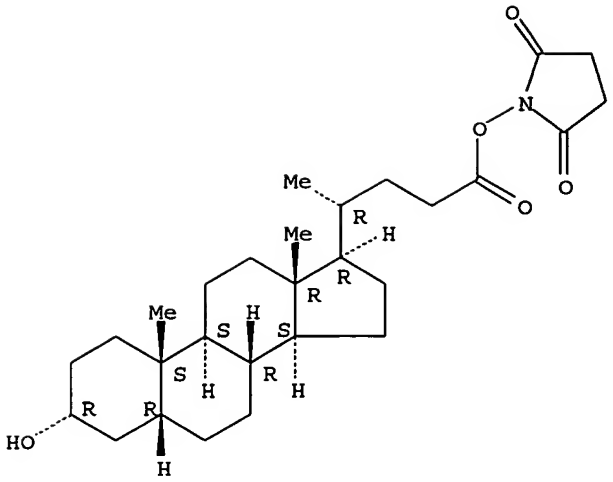


IT 104211-94-1DP, conjugates with insulin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lipophilic insulin derivs. soluble at physiol. pH with prolonged serum half-lives and biol. activity)

RN 104211-94-1 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[(3α,5β)-3-hydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

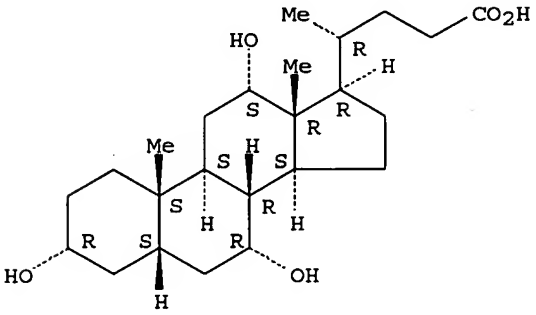
Absolute stereochemistry.



L40 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:722480 HCAPLUS
DN 132:313463
ED Entered STN: 12 Nov 1999
TI Thermosensitive self-aggregates prepared from cholic acid-**conjugated** amine-terminated poly(N-isopropylacrylamide) for drug delivery
AU Kim, I. S.; Kim, S. H.
CS College of Pharmacy, Chosun University, Kwangju, 501-759, S. Korea
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1999), 26th, 791-792
CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB Polymer micelles composed of cholic acid and aminoe-terminated thermoresponsive poly(N-isopropylacrylamide) were prepared and showed reversible thermal transition. Drug delivery systems using these thermosensitive micelles can be used for the site-specific drug delivery by modulating the temperature at the target site.
ST polyisopropylacrylamide nanoparticle micelle cholate drug delivery
IT **Drug delivery systems**
(nanoparticles, controlled-release; thermosensitive self-aggregates prepared from cholic acid-**conjugated** amine-terminated poly(N-isopropylacrylamide) for drug delivery)
IT Micelles
Self-association
(thermosensitive self-aggregates prepared from cholic acid-**conjugated** amine-terminated poly(N-isopropylacrylamide) for drug delivery)
IT **81-25-4DP**, Cholic acid, reaction products with amine-terminated poly(isopropylacrylamide) 25189-55-3DP, Poly(N-isopropylacrylamide), amine-terminated, reaction products with cholic acid
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thermosensitive self-aggregates prepared from cholic acid-**conjugated** amine-terminated poly(N-isopropylacrylamide) for drug delivery)
IT 53-86-1, Indomethacin
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thermosensitive self-aggregates prepared from cholic acid-

conjugated amine-terminated poly(N-isopropylacrylamide) for drug delivery)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anton, P; Makromol Chem 1993, V194, P1 HCAPLUS
(2) Bae, Y; J Controlled Release 1989, V9, P271 HCAPLUS
(3) Gao, Z; Macromolecules 1993, V26, P7353 HCAPLUS
(4) Guenoun, P; Macromolecules 1996, V29, P3965 HCAPLUS
(5) Xu, R; Macromolecules 1991, V24, P87 HCAPLUS
IT 81-25-4DP, Cholic acid, reaction products with amine-terminated poly(isopropylacrylamide)
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thermosensitive self-aggregates prepared from cholic acid-conjugated amine-terminated poly(N-isopropylacrylamide) for drug delivery)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:708452 HCAPLUS
DN 131:314185
ED Entered STN: 05 Nov 1999
TI Active hedgehog protein conjugate, process for its production and use
IN Esswein, Angelika; Lang, Kurt; Rueger, Petra; Seytter, Tilmann
PA Roche Diagnostics G.m.b.H., Germany
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K014-47
ICA C07K019-00
CC 63-5 (Pharmaceuticals)
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 953576	A1	19991103	EP 1999-108032	19990423 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 953575	A1	19991103	EP 1998-107911	19980430 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 335385	A	20000929	NZ 1999-335385	19990426 <--
MX 9903976	A	20000630	MX 1999-3976	19990428 <--
SG 80028	A1	20010417	SG 1999-2117	19990428 <--
US 6468978	B1	20021022	US 1999-301199	19990428 <--
CA 2269221	AA	19991030	CA 1999-2269221	19990429 <--

NO 9902090	A	19991101	NO 1999-2090	19990429	<--
ZA 9903009	A	19991101	ZA 1999-3009	19990429	<--
CN 1233616	A	19991103	CN 1999-106302	19990429	<--
AU 9925009	A1	19991111	AU 1999-25009	19990429	<--
AU 719797	B2	20000518			
JP 2000053699	A2	20000222	JP 1999-125005	19990430	<--
JP 3433136	B2	20030804			
BR 9903169	A	20001017	BR 1999-3169	19990430	<--
US 2003139574	A1	20030724	US 2002-278060	20021021	<--
US 6818623	B2	20041116			
PRAI EP 1998-107911	A	19980430	<--		
EP 1998-116733	A	19980903	<--		
US 1999-301199	A1	19990428	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
EP 953576	ICM	C07K014-47	
	ICA	C07K019-00	
EP 953576	ECLA	C07K014/47	<--
EP 953575	ECLA	C07K014/47	<--
US 6468978	NCL	514/021.000; 514/012.000; 530/350.000; 530/408.000; 530/409.000; 530/410.000	
	ECLA	C07K014/47	<--
US 2003139574	NCL	514/021.000; 514/012.000; 530/350.000; 530/408.000; 530/409.000; 530/410.000	
	ECLA	C07K014/47	<--

AB A hedgehog **conjugate** is disclosed which is characterized in that it contains: (a) a polypeptide composed of 10 to 30 hydrophobic amino acids and/or amino acids which form transmembrane helixes and are pos. charged, (b) 1 to 4 aliphatic, saturated or unsatd. hydrocarbon residues with a chain length of 10 to 24 C atoms and with a hydrophobic action or (c) a hydrophobic thio compound covalently bound to a hedgehog protein and which has a several-fold increased activity and is suitable as a pharmaceutical agent.

ST hedgehog protein lipid **conjugate** drug

IT Polysaccharides, uses
RL: NUU (Other use, unclassified); USES (Uses)
(acidic; active hedgehog protein **conjugates** for therapeutic use)

IT DNA sequences
Detergents
Drug delivery systems
Molecular cloning
Stabilizing agents
(active hedgehog protein **conjugates** for therapeutic use)

IT Primers (nucleic acid)
RL: PRP (Properties)
(active hedgehog protein **conjugates** for therapeutic use)

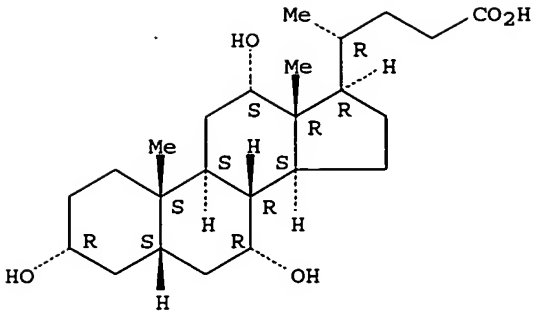
IT Alcohols, biological studies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(alkyl, hedgehog protein **conjugates**; active hedgehog protein **conjugates** for therapeutic use)

IT Fatty acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(hedgehog protein **conjugates**; active hedgehog protein **conjugates** for therapeutic use)

IT Hedgehog protein
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(lipid conjugates; active hedgehog protein conjugates for therapeutic use)
IT Dimerization
(of human sonic hedgehog protein; active hedgehog protein conjugates for therapeutic use)
IT Hedgehog protein
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(sonic, cloning of human; active hedgehog protein conjugates for therapeutic use)
IT 57-10-3DP, Palmitic acid, hedgehog protein conjugates
57-11-4DP, Stearic acid, hedgehog protein conjugates
60-33-3DP, Linoleic acid, hedgehog protein conjugates
112-80-1DP, Oleic acid, hedgehog protein conjugates
112-85-6DP, Behenic acid, hedgehog protein conjugates
143-07-7DP, Lauric acid, hedgehog protein conjugates
373-49-9DP, Palmitoleic acid, hedgehog protein conjugates
463-40-1DP, Linolenic acid, hedgehog protein conjugates
506-30-9DP, Arachidic acid, hedgehog protein conjugates
506-32-1DP, Arachidonic acid, hedgehog protein conjugates
544-63-8DP, Myristic acid, hedgehog protein conjugates
1249-81-6DP, Thiocholesterol, hedgehog protein conjugates
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(active hedgehog protein conjugates for therapeutic use)
IT 145-63-1, Suramin 9005-49-6, Heparin, uses
RL: NUU (Other use, unclassified); USES (Uses)
(active hedgehog protein conjugates for therapeutic use)
IT 361-09-1, Sodium cholate 2281-11-0, Zwittergent 3-16
9002-93-1, Triton x 100 9005-65-6, Tween 80 14933-09-6, Zwittergent 3-14 41444-50-2, Octyl glucoside 75621-03-3, Chaps
RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)
(active hedgehog protein conjugates for therapeutic use)
IT 3867-67-2P 17450-31-6P 26227-65-6P 60988-34-3P 69205-88-5P
69205-89-6P 136911-91-6P 247900-73-8P 247900-74-9P
247900-75-0P 247900-76-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(active hedgehog protein conjugates for therapeutic use)
IT 1763-10-6, Palmitoyl-CoA
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling agent; active hedgehog protein conjugates for therapeutic use)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Beachy, P; WO 9830576 A 1998 HCAPLUS
(2) Farese, R; TRENDS IN GENETICS 1998, V14(3), P115 HCAPLUS
(3) Hammerschmidt, M; TRENDS IN GENETICS 1997, V13(1), P14 HCAPLUS
(4) Hancock; CELL 1990, V63, P133 HCAPLUS
(5) Harvard College; WO 9518856 A 1995 HCAPLUS
(6) Mohler; DEVELOPMENT 1992, V115, P957 HCAPLUS
(7) Porter; CELL 1996, V86, P21 HCAPLUS
(8) Porter; SCIENCE 1996, V274, P255 HCAPLUS
IT 361-09-1, Sodium cholate
RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)
(active hedgehog protein conjugates for therapeutic use)
RN 361-09-1 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, monosodium salt, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

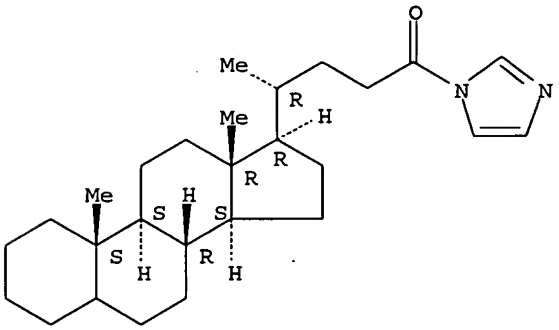
Absolute stereochemistry.



● Na

IT 247900-74-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(active hedgehog protein conjugates for therapeutic use)
RN 247900-74-9 HCAPLUS
CN 1H-Imidazole, 1-(24-oxocholan-24-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:208387 HCAPLUS
DN 128:286354
ED Entered STN: 13 Apr 1998
TI Methods and compositions for lipidization of hydrophilic molecules
IN Shen, Wei-Chiang; Wang, Jinghua
PA University of Southern California, USA; Shen, Wei-Chiang; Wang, Jinghua
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9813007	A2	19980402	WO 1997-US17282	19970926 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,

```
            UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
            GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
            GN, ML, MR, NE, SN, TD, TG
     CA 2267179          AA    19980402    CA 1997-2267179        19970926 <--
     AU 9745967          A1    19980417    AU 1997-45967          19970926 <--
     AU 737865           B2    20010906
     CN 1235594          A     19991117    CN 1997-199191         19970926 <--
     CN 1127477          B     20031112
     EP 1023316          A2    20000802    EP 1997-944483         19970926 <--
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
     BR 9712128          A     20001212    BR 1997-12128          19970926 <--
     JP 2002515883       T2    20020528    JP 1998-515933         19970926 <--
     NO 9901465          A     19990510    NO 1999-1465           19990325 <--
     KR 2000048608       A     20000725    KR 1999-702543         19990325 <--
PRAI US 1996-721306      A     19960926  <--
     US 1997-49499P      P     19970613  <--
     US 1996-77177P      P     19960926  <--
     WO 1997-US17282     W     19970926  <--
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------  -----  ----------------------------------------------
 WO 9813007      ICM    A61K
 WO 9813007      ECLA   A61K047/48H4                                    <--
OS   MARPAT 128:286354
AB   Fatty acid derivs. of disulfide-containing compds. (for example,
     disulfide-containing peptides or proteins) comprising fatty acid-
     conjugated products with a disulfide linkage are employed for
     delivery of the compds. to mammalian cells.  This modification markedly
     increases the absorption of the compds. by mammalian cells relative to the
     rate of absorption of the unconjugated compds., as well as
     prolonging blood and tissue retention of the compds.  Moreover, the
     disulfide linkage in the conjugate is quite labile in vivo and
     thus facilitates intracellular or extracellular release of the intact
     compds. from the fatty acid moieties.  N-palmitoyl-2-pyridyldithiocysteine
     was prepared and conjugated to BBI hydrophilic protein and its
     transport and biodistribution studied.
ST   lipidization hydrophilic compd delivery; fatty acid deriv protein peptide
     delivery
IT   Drug delivery systems
        (lipidization of hydrophilic mols. for peptide or protein delivery)
IT   Disulfides
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (lipidization of hydrophilic mols. for peptide or protein delivery)
IT   Drug delivery systems
        (liposomes; lipidization of hydrophilic mols. for peptide or protein
        delivery)
IT   Proteins, general, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
        (reaction products with palmitoylpyridyldithiocysteine, lipidization of
        hydrophilic mols. for peptide or protein delivery)
IT   Oligonucleotides
     Peptides, biological studies
     Proteins, specific or class
     RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
        (reaction products, with fatty acids; lipidization of hydrophilic mols.
        for peptide or protein delivery)
IT   Fatty acids, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); PROC (Process); USES (Uses)
```

(reaction products, with proteins and peptides; lipidization of hydrophilic mols. for peptide or protein delivery)

IT 112-80-1DP, Oleic acid, derivative, reaction products with peptides and proteins 1200-22-2DP, Lipoic acid, reaction products with acyclovir and palmitic acid derivative 9003-99-0DP, Peroxidase, reaction products with palmitic acid derivative 16679-58-6DP, Desmopressin, reaction products with palmitic acid derivative 47931-85-1DP, Salmon calcitonin, reaction products with palmitic acid derivative 59277-89-3DP, Acyclovir, reaction products with lipoic acid and palmitic acid derivative 171735-25-4DP, reaction products with peptides and proteins **174069-00-2DP**, reaction products with palmitic acid derivative
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(lipidization of hydrophilic mols. for peptide or protein delivery)

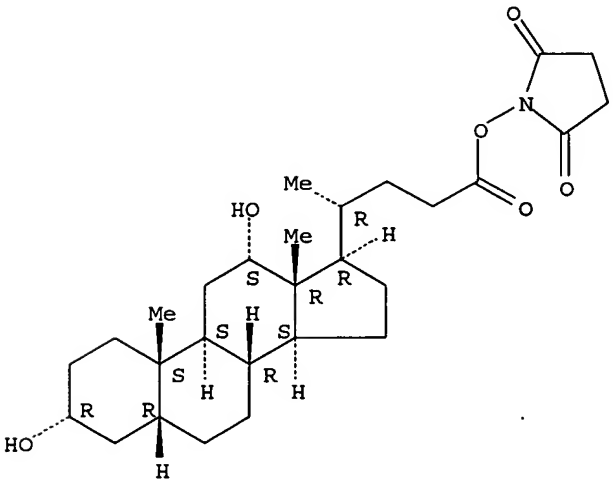
IT 52-90-4, L-Cysteine, reactions 83-44-3, Deoxycholic acid 2127-03-9, Pyridine, 2,2'-Dithiobis- 6066-82-6, N-Hydroxysuccinimide 68181-17-9, SPDP
RL: RCT (Reactant); RACT (Reactant or reagent)
(lipidization of hydrophilic mols. for peptide or protein delivery)

IT 14464-31-4P, N-Hydroxysuccinimide palmitate 88442-68-6P 171735-25-4P **174069-00-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lipidization of hydrophilic mols. for peptide or protein delivery)

IT **174069-00-2DP**, reaction products with palmitic acid derivative
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(lipidization of hydrophilic mols. for peptide or protein delivery)

RN 174069-00-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

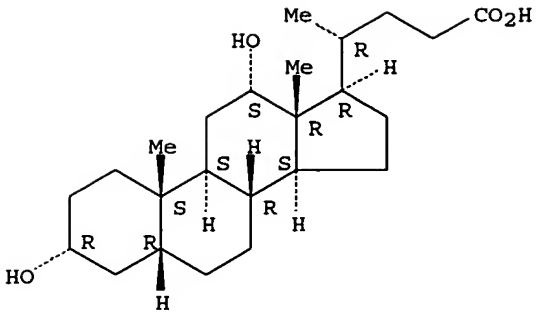
Absolute stereochemistry.



IT 83-44-3, Deoxycholic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(lipidization of hydrophilic mols. for peptide or protein delivery)

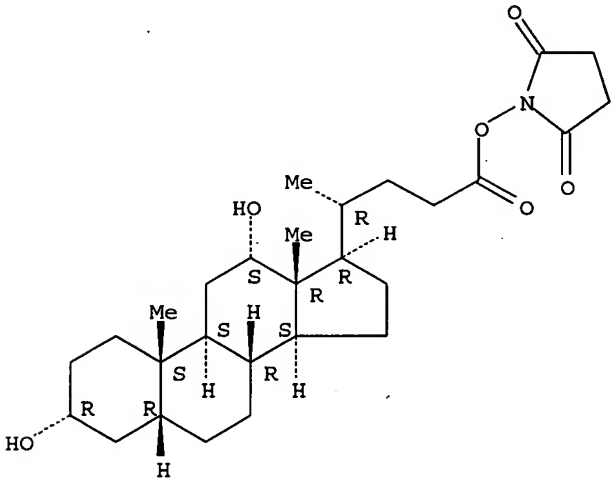
RN 83-44-3 HCAPLUS
CN Cholan-24-oic acid, 3,12-dihydroxy-, (3α,5β,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 174069-00-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lipidization of hydrophilic mols. for peptide or protein delivery)
RN 174069-00-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

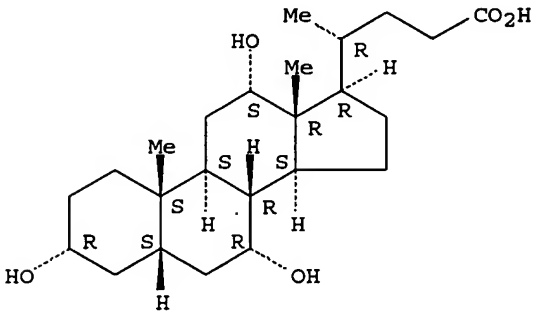
Absolute stereochemistry.



L40 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:463447 HCAPLUS
DN 127:99659
ED Entered STN: 24 Jul 1997
TI Oral peptide delivery using the intestinal bile acid transporter
AU Swaan, P. W.; Szoka, F. C., Jr.; Oie, S.
CS University of California at San Francisco, CA, 94143-0446, USA
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 7-8
CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
AB The intestinal absorption of peptides was increased by coupling to the 24 position of the steroid nucleus in cholic acid.
ST bile acid peptide delivery intestine
IT Drug delivery systems
Intestine

(oral peptide delivery using intestinal bile acid transporter)
IT Bile acids
Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral peptide delivery using intestinal bile acid transporter)
IT 81-25-4D, Cholic acid, peptide conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral peptide delivery using intestinal bile acid transporter)
IT 81-25-4D, Cholic acid, peptide conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral peptide delivery using intestinal bile acid transporter)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alph
a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:443336 HCAPLUS
DN 127:55909
ED Entered STN: 17 Jul 1997
TI Sulfate conjugates of ursodeoxycholic acid, and their beneficial use in inflammatory disorders and other applications
IN Setchell, Kenneth D. R.
PA Children's Hospital Medical Center, Philadelphia, USA
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-575
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9718816	A2	19970529	WO 1996-US18487	19961119 <--
WO 9718816	A3	19970626		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5763435	A	19980609	US 1995-560992	19951121 <--
CA 2238040	AA	19970529	CA 1996-2238040	19961119 <--
CA 2238040	C	20040713		
AU 9677377	A1	19970611	AU 1996-77377	19961119 <--
AU 709594	B2	19990902		
EP 871452	A2	19981021	EP 1996-940516	19961119 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

	CN 1211185	A	19990317	CN 1996-199708	19961119	<--
	JP 2000500764	T2	20000125	JP 1997-519828	19961119	<--
	BR 9611606	A	20001024	BR 1996-11606	19961119	<--
	PL 186393	B1	20040130	PL 1996-326931	19961119	<--
	US 6251884	B1	20010626	US 1998-28036	19980224	<--
	NO 9802281	A	19980708	NO 1998-2281	19980519	<--
PRAI	US 1995-560992	A	19951121	<--		
	WO 1996-US18487	W	19961119	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9718816	ICM	A61K031-575	
WO 9718816	ECLA	A61K031/575	<--
US 5763435	NCL	514/182.000	
	ECLA	A61K031/575	<--
US 6251884	NCL	514/182.000; 514/169.000	
	ECLA	A61K031/575	<--

AB Pharmaceutically acceptable compns. including a sulfate of ursodeoxycholic acid (I), glycoursodeoxycholic acid, or tauroursodeoxycholic acid and a pharmacol. acceptable carrier are useful for treatment of mammals for disorders including inflammation of the gastrointestinal tract, colon cancer, rectum cancer, ulcerative colitis, adenomatous polyps, familial polyposis, hepatitis, etc. These compns. may be used to improve liver function or serum biochem. in liver disease, to increase bile flow, or to decrease biliary secretion of phospholipid or cholesterol. An isolated organ may be maintained in vitro by perfusion with a I sulfate. Thus, I was condensed with tert-butyldimethylsilyl chloride to form the 3-tert-butyldimethylsilyl ether, then with Ac2O to form I 3-tert-butyldimethylsilyl ether 7-acetate, hydrolyzed with HCl to I 7-acetate, condensed with ClSO3H to form I 7-acetate 3-sulfate, converted to the di-Na salt, and saponified with methanolic NaOH to I 3-sulfate.

ST ursodeoxycholate sulfate inflammation inhibitor; colon cancer ursodeoxycholate sulfate; rectum cancer ursodeoxycholate sulfate; liver disease ursodeoxycholate sulfate

IT Intestine, neoplasm
(colon, inhibitors; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Antitumor agents
(colon; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Digestive tract
(disease, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Anti-inflammatory agents
(gastrointestinal; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Solutions
(isotonic solns., for organ perfusion; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine
(large, disease, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine
Kidney
Lung
Organ preservation
(perfusion fluid for; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, neoplasm

(polyp, adenomatous; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, neoplasm
Intestine, neoplasm
(rectum, inhibitors; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Antitumor agents
Antitumor agents
(rectum; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Phospholipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(secretion of, in bile; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, disease
Intestine, disease
(small, inflammation; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Choleretics
Hepatitis
Liver, disease
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Intestine, disease
(ulcerative colitis; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT Biological transport
(uptake, of ursodeoxycholic acid by intestine, inhibition of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 434-13-9, Lithocholic acid
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(formation from ursodeoxycholate; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 128-13-2, Ursodeoxycholic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(intestinal absorption of; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(secretion of, in bile; sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 71781-68-5P 191286-16-5P 191286-18-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 68780-73-4, Ursodeoxycholic acid 3-sulfate 74723-13-0, Tauroursodeoxycholic acid 3-sulfate 74723-14-1 74723-15-2 74723-16-3 88426-32-8 109333-29-1 133429-88-6, Glycoursodeoxycholic acid 3-sulfate 191286-12-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 474-25-9, Chenodeoxycholic acid 2393-58-0, α-Muricholic acid 2393-59-1, β-Muricholic acid 6830-03-1, ω-Muricholic acid 114183-56-1 114183-57-2 163750-00-3

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

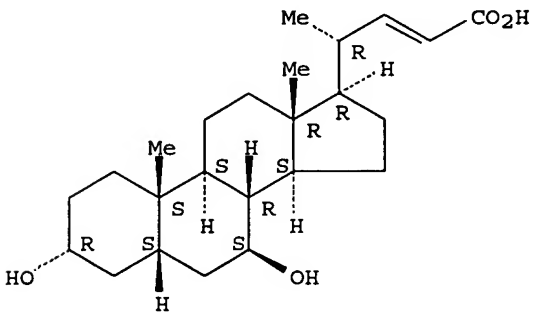
IT 18162-48-6, tert-Butyldimethylsilyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 71781-57-2P 71781-58-3P 75672-25-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

IT 163750-00-3
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(sulfate conjugates of ursodeoxycholic acid for treatment of inflammatory disorders)

RN 163750-00-3 HCAPLUS
CN Chol-22-en-24-oic acid, 3,7-dihydroxy-, (3α,5β,7β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L40 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:372273 HCAPLUS
DN 126:347323
ED Entered STN: 14 Jun 1997
TI Buccal delivery of glucagon-like insulinotropic peptides (GLPs)
IN Heiber, Sonia J.; Ebert, Charles D.; Gutniak, Mark K.
PA Theratech, Inc., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-70
ICS A61L015-16
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9715296	A1	19970501	WO 1996-US16890	19961022 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
	US 5766620	A	19980616	US 1995-553807	19951023 <--

CA 2235369	AA	19970501	CA 1996-2235369	19961022	<--
AU 9674647	A1	19970515	AU 1996-74647	19961022	<--
AU 716038	B2	20000217			
EP 859606	A1	19980826	EP 1996-936815	19961022	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1202820	A	19981223	CN 1996-198618	19961022	<--
BR 9611139	A	19990406	BR 1996-11139	19961022	<--
JP 11513982	T2	19991130	JP 1996-516712	19961022	<--
TW 416854	B	20010101	TW 1996-85112962	19961022	<--
ZA 9608909	A	19970528	ZA 1996-8909	19961023	<--
US 5863555	A	19990126	US 1997-964731	19971105	<--
PRAI US 1995-553807	A	19951023	<--		
WO 1996-US16890	W	19961022	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9715296	ICM	A61K009-70
	ICS	A61L015-16
US 5766620	NCL	424/436.000; 424/435.000; 514/772.300; 514/772.600; 514/774.000; 514/777.000; 514/781.000
	ECLA	A61K009/00M18D; A61K038/26 <--
US 5863555	NCL	424/435.000; 514/772.300; 514/772.600; 514/774.000; 514/777.000; 514/781.000
	ECLA	A61K038/26 <--

AB Drug delivery systems for administering a GLP to the buccal mucosa for transmucosal drug delivery comprise a drug composition containing effective amts. of the GLP and a permeation enhancer, and means for maintaining the drug composition in a drug-transferring relation with the buccal mucosa. These systems can be in free form, such as creams, gels, and ointments, or can comprise a device of determined phys. form, such as tablets, patches, and troches. A preferred GLP is GLP-1(7-36) amide. Thus, a gingival bilayer tablet was prepared comprising an active layer and an adhesive layer. The adhesive layer was prepared by mixing polyethylene oxide 70, Carbopol 934P 20, and compressible xylitol/CM-cellulose filler 10 weight parts, granulating with EtOH, sieving, drying, mixing with stearic acid 0.25 and mint flavor 0.06 weight%, and compression. To prepare the active layer, mannitol 49.39, hydroxypropylcellulose 34.33, and Na taurocholate 15.00 weight% were mixed, granulated with EtOH, sieved, dried, combined with GLP-1(7-36) amide 0.91, FD&C Yellow Number 6HT 0.06, Mg stearate 0.25, and mint flavor 0.06 weight%; 50 mg of this mixture was compressed onto 50 mg adhesive layer.

ST glucagonlike insulinotropic peptide buccal tablet; mouth absorption glucagonlike insulinotropic peptide

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C2-3, permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT Glycols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C3-4; buccal delivery of glucagon-like insulinotropic peptides)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesive containing; buccal delivery of glucagon-like insulinotropic peptides)

IT Caseins, biological studies
Gelatins, biological studies
Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesives containing; buccal delivery of glucagon-like insulinotropic peptides)

IT Adhesives
(biol.; buccal delivery of glucagon-like insulinotropic peptides)

IT Antidiabetic agents
Gingiva
Permeation enhancers
(buccal delivery of glucagon-like insulinotropic peptides)

IT Sulfonylureas
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
(buccal; buccal delivery of glucagon-like insulinotropic peptides)

IT Steroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detergents, as permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT Cell membrane
(disrupting agents for; buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
(gels; buccal delivery of glucagon-like insulinotropic peptides)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic, adhesive containing; buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
(lozenges; buccal delivery of glucagon-like insulinotropic peptides)

IT Mouth
(mucosa; buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
(ointments, creams; buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
(ointments; buccal delivery of glucagon-like insulinotropic peptides)

IT Chelating agents
Solvents
Surfactants
(permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT Bile salts
Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT Vinyl compounds, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymers, adhesives containing; buccal delivery of glucagon-like insulinotropic peptides)

IT Detergents
(steroidal, as permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT **Drug delivery systems**
Drug delivery systems
(tablets, buccal; buccal delivery of glucagon-like insulinotropic peptides)

IT 79-10-7D, 2-Propenoic acid, esters, polymers, biological studies
79-10-7D, 2-Propenoic acid, polymers, biological studies 557-75-5D, Ethenol, polymers, biological studies 9000-30-0, Guar gum 9000-69-5, Pectin 9003-39-8, PVP 9004-32-4 9004-54-0, Dextran, biological studies 9004-57-3, Ethylcellulose 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9005-25-8, Starch, biological studies 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adhesive containing; buccal delivery of glucagon-like insulinotropic peptides)

IT 107444-51-9 118549-37-4, Insulinotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal delivery of glucagon-like insulinotropic peptides)

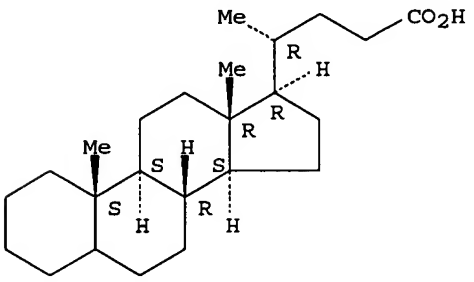
IT 67-68-5, biological studies 68-12-2, biological studies 102-76-1, Triacetin 108-32-7, Propylene carbonate 110-27-0, Isopropyl myristate 111-82-0, Methyl laurate 112-80-1, Oleic acid, biological studies 122-32-7, Glycerol trioleate 127-19-5 143-28-2, Oleyl alcohol 145-42-6, Sodium taurocholate 151-21-3, SDS, biological studies 872-50-4, N-Methylpyrrolidone, biological studies 3445-11-2, N-(2-Hydroxyethyl)-2-pyrrolidinone 5306-85-4, Dimethyl isosorbide 25496-72-4, Glycerol monooleate 25637-84-7, Glycerol dioleate 27194-74-7, Propylene glycol monolaurate 27215-38-9, Glycerol monolaurate 31566-31-1, Glycerol monostearate 59227-89-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancer; buccal delivery of glucagon-like insulinotropic peptides)

IT 107-35-7D, Taurine, bile acid conjugates, salts 12441-09-7D, Sorbitan, esters 25312-65-6D, Cholanic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

IT 25312-65-6D, Cholanic acid, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(permeation enhancers; buccal delivery of glucagon-like insulinotropic peptides)

RN 25312-65-6 HCAPLUS
CN Cholan-24-oic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:218959 HCAPLUS
DN 126:308684
ED Entered STN: 04 Apr 1997
TI Use of the intestinal bile acid transporter for the uptake of cholic acid conjugates with HIV-1 protease inhibitory activity
AU Kagedahle, Matts; Swaan, Peter W.; Redemann, Carl T.; Tang, Mary; Craik, Charles S.; Szoka, Francis C., Jr.; Oie, Svein
CS Dep. Pharmacy Pharmaceutical Chem., Univ. California, San Francisco, CA, 94143-0446, USA
SO Pharmaceutical Research (1997), 14(2), 176-180
CODEN: PHREEB; ISSN: 0724-8741
PB Plenum
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
AB The purpose of this study was to investigate the ability of the human intestinal bile acid transporter to transport cholic acid conjugates with potential HIV-1 protease inhibitory activity. Cholic acid was conjugated at the 24 position of the sterol nucleus with various amino acids and amino acid analogs. The CaCo-2 cell line was used as a model to investigate the interaction of these bile acid conjugates with the human intestinal bile acid transporter. Interaction between the carrier and the conjugates was

quantified by inhibition of taurocholic acid transport and confirmed by transport of radiolabeled conjugates in this cell line. The highest interaction with the transporter, as quantified by inhibition of taurocholic acid transport, occurred when a single neg. charge was present around the 24 to 29 region of the sterol nucleus. A second neg. charge or a pos. charge significantly reduced the interaction. Transport of radiolabeled cholyl-L-Lys-ε-tBOC ester and cholyl-D-Asp-β-benzyl ester was inhibited by taurocholic acid. Of all tested compds., only cholyl-D-Asp-β-benzyl ester showed modest HIV-1 protease inhibitory activity with an IC50 of 125 μM. Cholic acid-amino acid conjugates with appropriate stereochem. are recognized and transported by the human bile acid transporter and show modest HIV-1 protease inhibitory activity. Transport of these conjugates by the bile acid carrier is influenced by charge and hydrophobicity around the 24 position of the sterol nucleus.

ST bile amino acid conjugate intestine transport; HIV1 protease inhibition cholate conjugate AIDS

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(conjugates, with amino acids; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Amino acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(conjugates, with bile acids; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Biological transport
(drug; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Drug delivery systems
(oral; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Bile acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transporter; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Biological transport
(uptake; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT Anti-AIDS agents
Hydrophobicity
Intestine
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(HIV-1; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 7440-23-5, Sodium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bile acid transport dependent on; use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT 2365-14-2P 28071-39-8P, Cholyl-L-lysine
73386-01-3P 89311-00-2P 106335-70-0P
189261-12-9P 189261-13-0P 189261-14-1P
189261-15-2P 189282-94-8P 189282-95-9P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological

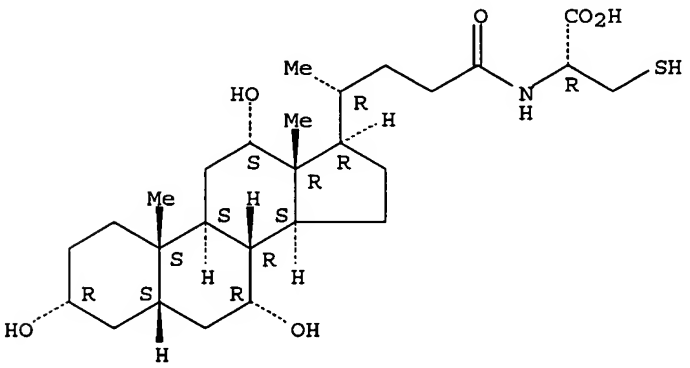
process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT **81-25-4D**, Cholic acid, conjugates with amino acids
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

IT **2365-14-2P 28071-39-8P**, Cholyl-L-lysine
73386-01-3P 89311-00-2P 106335-70-0P
189261-12-9P 189261-13-0P 189261-14-1P
189261-15-2P 189282-94-8P 189282-95-9P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)

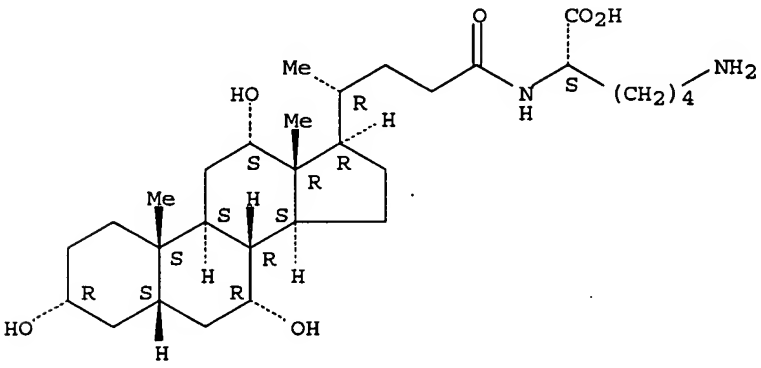
RN 2365-14-2 HCAPLUS
CN L-Cysteine, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 28071-39-8 HCAPLUS
CN L-Lysine, N2-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

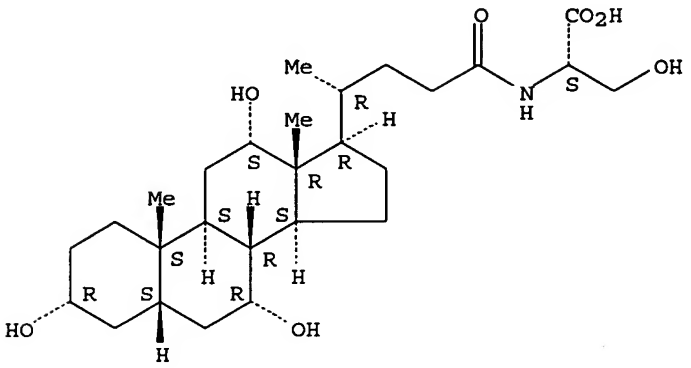
Absolute stereochemistry.



RN 73386-01-3 HCAPLUS

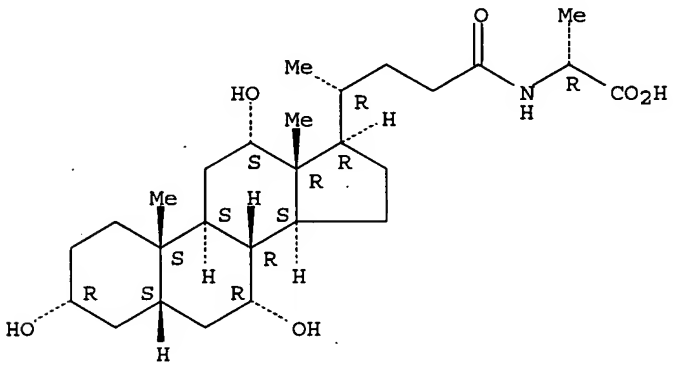
CN L-Serine, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



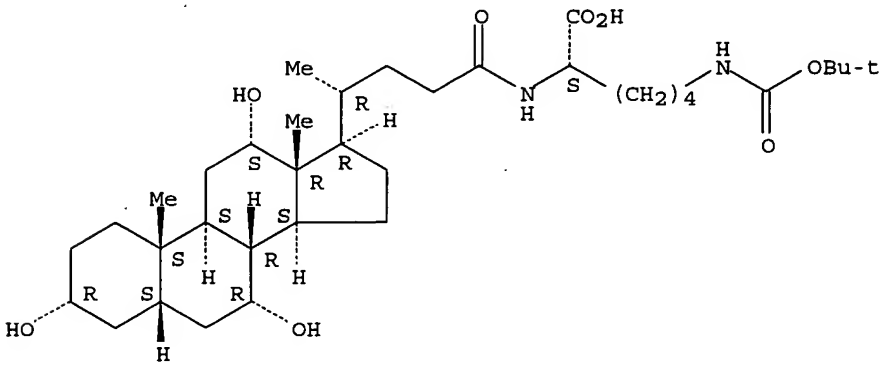
RN 89311-00-2 HCAPLUS
CN D-Alanine, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



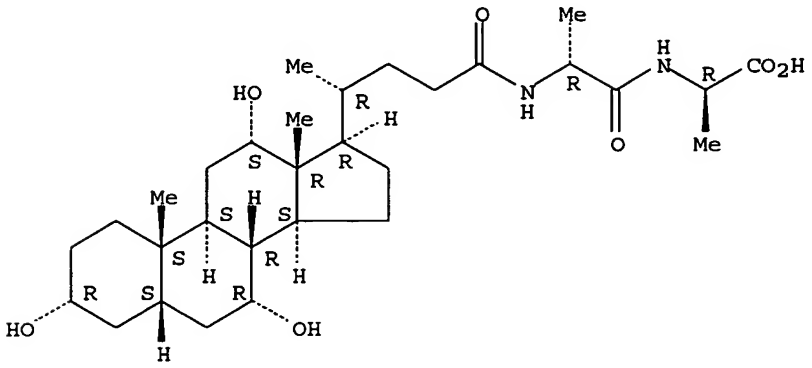
RN 106335-70-0 HCAPLUS
CN L-Lysine, N6-[(1,1-dimethylethoxy)carbonyl]-N2-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



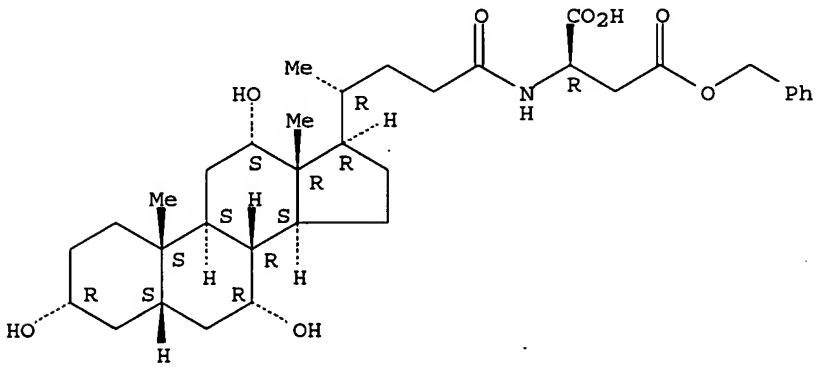
RN 189261-12-9 HCAPLUS
CN D-Alanine, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



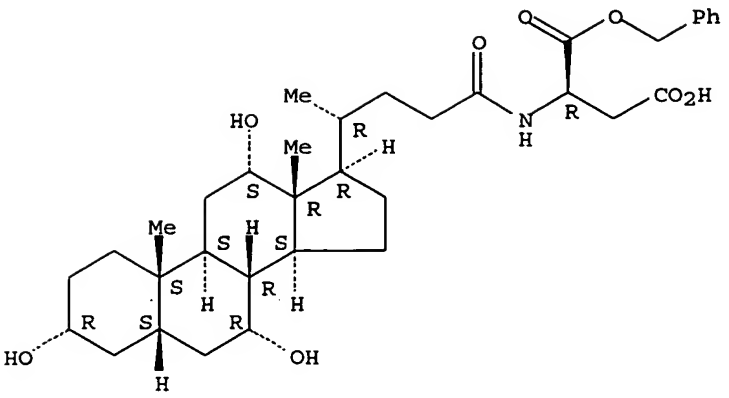
RN 189261-13-0 HCAPLUS
CN D-Aspartic acid, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 4-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



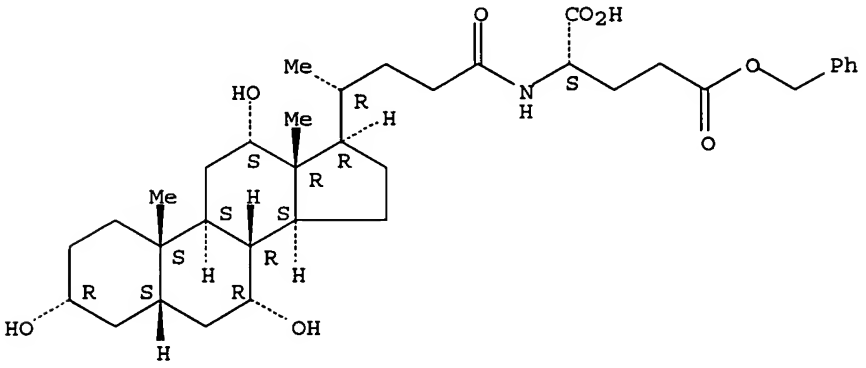
RN 189261-14-1 HCAPLUS
CN D-Aspartic acid, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



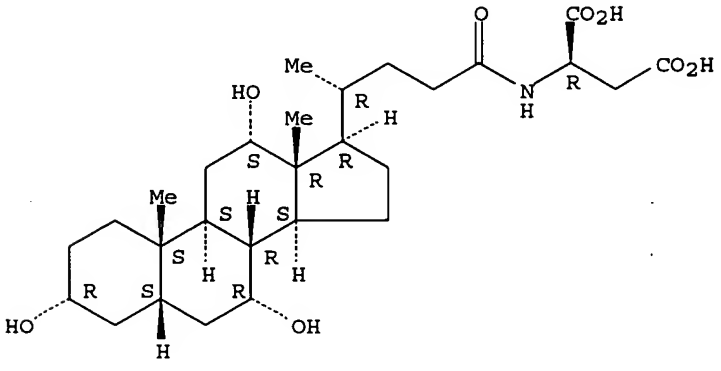
RN 189261-15-2 HCAPLUS
CN L-Glutamic acid, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



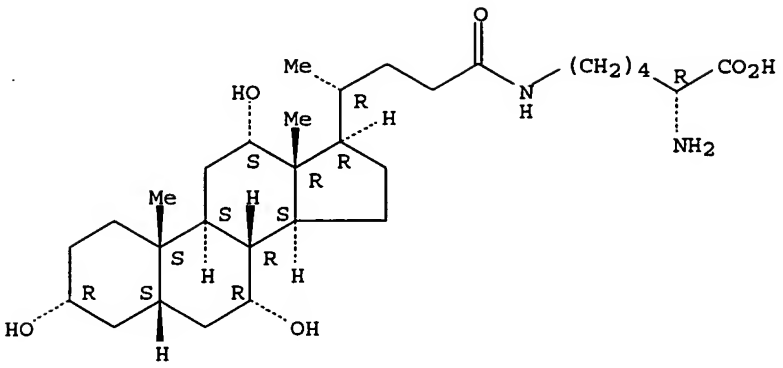
RN 189282-94-8 HCAPLUS
CN D-Aspartic acid, N-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



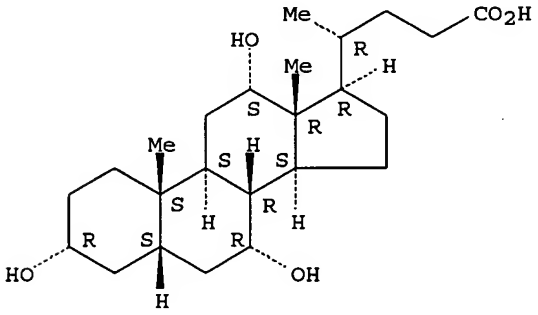
RN 189282-95-9 HCAPLUS
CN D-Lysine, N6-[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 81-25-4D, Cholic acid, conjugates with amino acids
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of intestinal bile acid transporter for uptake of cholic acid conjugates with HIV-1 protease inhibitory activity)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alph a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:721131 HCAPLUS
DN 123:322102
ED Entered STN: 05 Aug 1995
TI Acylated derivatives of human insulin with improved solubility and stability for treatment of diabetes
IN Havelund, Svend; Halstroem, John Broberg; Jonassen, Ib; Andersen, Asser Sloth; Markussen, Jan
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-62
ICS A61K038-28
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 2, 3
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

```
PI   WO 9507931          A1    19950323    WO 1994-DK347          19940916 <--
       W:  AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG,
           KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU,
           SD, SI, SK, TJ, TT, UA, US, UZ, VN
       RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,
           NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     ZA 9407187          A     19950317    ZA 1994-7187           19940916 <--
     CA 2171424          AA    19950323    CA 1994-2171424        19940916 <--
     CA 2171424          C     20020604
     AU 9476520          A1    19950403    AU 1994-76520          19940916 <--
     AU 682061           B2    19970918
     CN 1133598          A     19961016    CN 1994-193852         19940916 <--
     CN 1056618          B     20000920
     BR 9407508          A     19970107    BR 1994-7508           19940916 <--
     HU 75991            A2    19970528    HU 1996-676            19940916 <--
     HU 217684           B     20000328
     EP 792290           A1    19970903    EP 1994-926816         19940916 <--
     EP 792290           B1    20010829
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     RO 112873           B1    19980130    RO 1996-583            19940916 <--
     JP 3014764          B2    20000228    JP 1995-508923         19940916 <--
     JP 09502867         T2    19970325
     JP 2000060556       A2    20000229    JP 1999-221632         19940916 <--
     PL 178466           B1    20000531    PL 1994-313444         19940916 <--
     IL 110977           A1    20000629    IL 1994-110977         19940916 <--
     CZ 287945           B6    20010314    CZ 1996-789            19940916 <--
     RU 2164520          C2    20010327    RU 1996-108249         19940916 <--
     EP 1132404          A2    20010912    EP 2001-112992         19940916 <--
     EP 1132404          A3    20020327
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
            SI, LT
     AT 204882           E     20010915    AT 1994-926816         19940916 <--
     PT 792290           T     20020130    PT 1994-926816         19940916 <--
     ES 2163451          T3    20020201    ES 1994-926816         19940916 <--
     SK 282495           B6    20020205    SK 1996-324            19940916 <--
     JP 2002308899       A2    20021023    JP 2001-385921         19940916 <--
     FI 9601220          A     19960514    FI 1996-1220           19960315 <--
     NO 9601070          A     19960515    NO 1996-1070           19960315 <--
     AU 9748461          A1    19980219    AU 1997-48461          19971218 <--
     AU 745983           B2    20020411    AU 2000-51960          20000811 <--
PRAI DK 1993-1044        A     19930917  <--
     US 1994-190829      A     19940202  <--
     EP 1994-926816      A3    19940916  <--
     JP 1995-508923      A3    19940916  <--
     JP 1999-221632      A3    19940916  <--
     WO 1994-DK347       W     19940916  <--
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------  -----  ----------------------------------------------------
 WO 9507931      ICM    C07K014-62
                 ICS    A61K038-28
 WO 9507931      ECLA   C07K014/62                                          <--
 EP 1132404      ECLA   C07K014/62                                          <--
AB   Novel human insulin derivs. with improved solubility and a protracted profile
     of action are described for use in the treatment of diabetes.  These
     analogs have amino acid substitutions at amino acids A21 and B3 (any amino
     acid except Lys, Arg, or Cys); PheB1 may be deleted and B30 is substituted
     by a C10-24 lipophilic amino acid or any naturally occurring amino acid
     except Lys, Arg, or Cys; if B30 is a lipophilic amino acid, then the
     ε-NH2 group of LysB29 is acylated with a C≤5 carboxylic
     acid.  They may be used in the treatment of diabetes in several
     pharmaceutical compns. presented.  Chemical preparation of some of these analogs
     and the manufacture of the amino acid-substituted A and B chains by expression
     of the cloned cDNAs is demonstrated.
ST   human insulin sequence acylation diabetes pharmaceutical
IT   Protein sequences
```

(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Solubility
(at physiol. pH; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Acetyl group
Formyl group
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Fatty acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Diabetes mellitus
(insulin pharmaceutical composition for treatment of; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Plasmid and Episome
(pAK-series and pKFN1627 and pEA-series; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(C5, insulins modified with; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Deoxyribonucleic acid sequences
(complementary, acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(di-, C<6, insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT **Pharmaceutical dosage forms**
(**injections**, insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT Functional groups
(propionyl, insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 11061-68-0DP, Insulin (human), amino acid-substituted and lipophilic amino acid-containing derivs.
RL: BPN (Biosynthetic preparation); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 9002-07-7D, Trypsin, immobilized 123175-82-6D, Proteinase, lysine-specific, immobilized
RL: CAT (Catalyst use); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 14464-31-4, Palmitic acid N-hydroxysuccinimide ester 69888-86-4 88404-23-3 104943-24-0 165893-02-7 165893-03-8 **168986-19-4** 168986-20-7 169142-69-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-17-2P 168986-18-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 23713-49-7DP, Zn2+, complexes with insulin derivs., preparation

RL: SPN (Synthetic preparation); PREP (Preparation)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 169535-16-4P 169535-18-6P 169535-20-0P 169535-22-2P 169535-28-8P
169535-30-2P 169535-32-4P 169535-34-6P 169535-36-8P 169535-38-0P
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 120177-51-7P 169148-61-2P 169148-75-8P
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 39416-73-4P 169148-55-4DP, zinc complexes 169148-56-5DP, zinc complexes 169148-57-6P 169148-58-7P 169148-59-8P 169148-60-1P
169148-62-3DP, zinc complexes 169148-63-4P 169148-64-5P 169148-65-6P
169148-66-7P 169148-67-8P 169148-68-9P 169148-69-0P 169148-70-3P
169148-71-4P 169148-72-5DP, zinc complexes 169148-72-5P 169148-73-6P
169148-74-7P
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 141537-81-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-14-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 7452-59-7, n-Octyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation active ester derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 14565-47-0 22102-66-5 104211-94-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation chemical modified insulin analogs; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 108-30-5, Succinic anhydride, reactions 158627-30-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation myristic acid derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-15-0P 168986-16-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation myristic acid derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 11075-17-5, Carboxypeptidase A
RL: CAT (Catalyst use); USES (Uses)
(in preparation of insulin derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 51-49-0, D-Thyroxine 68528-80-3, Disuccinimidyl suberate
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation thyroxine derivative for conjugation to insulin; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 110-15-6, Butanedioic acid, reactions 143-07-7, Dodecanoic acid, reactions 638-53-9, Tridecanoic acid 7145-63-3, 2-Aminotetradecanoic

acid 7769-79-1, Hexadecanoic acid, 2-amino- 17702-88-4, 2-Aminodecanoic acid 35237-37-7, 2-Aminododecanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin derivs. containing; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 544-63-8, Tetradecanoic acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(insulin modification by; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

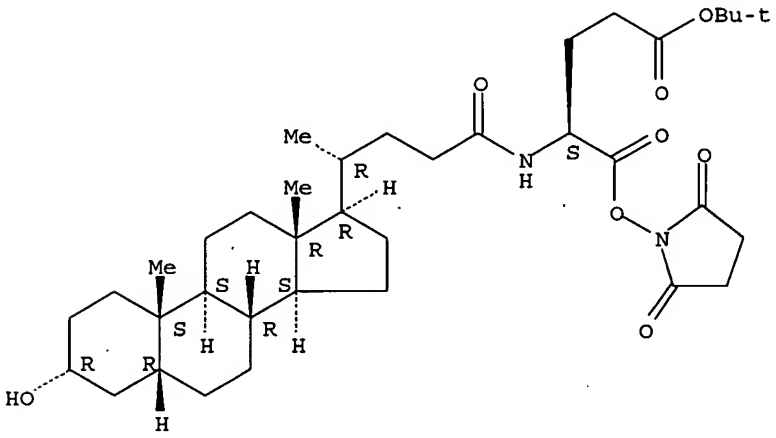
IT 169535-17-5P 169535-19-7P 169535-21-1P 169535-23-3P 169535-24-4P 169535-25-5P 169535-26-6P 169535-27-7P 169535-29-9P 169535-31-3P 169535-33-5P 169535-35-7P 169535-37-9P 169535-39-1P
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 24424-99-5, Di-tert-butyl pyrocarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(protecting group, in preparation of insulin derivs.; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

IT 168986-19-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

RN 168986-19-4 HCAPLUS
CN Pentanoic acid, 5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-[[(3α,5β)-3-hydroxy-24-oxocholan-24-yl]amino]-5-oxo-, 1,1-dimethylethyl ester, (4S)- (9CI) (CA INDEX NAME)

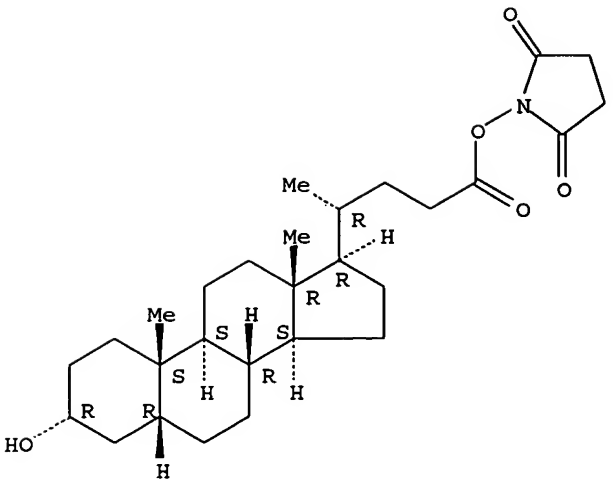
Absolute stereochemistry.



IT 104211-94-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(in preparation chemical modified insulin analogs; acylated derivs. of human insulin with improved solubility and stability for treatment of diabetes)

RN 104211-94-1 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[(3α,5β)-3-hydroxy-24-oxocholan-24-yl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



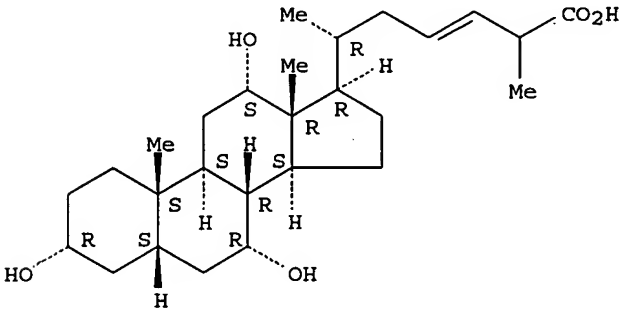
L40 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:96130 HCAPLUS
DN 122:3980
ED Entered STN: 08 Nov 1994
TI Bile salts of the toad, Bufo marinus: characterization of a new unsaturated higher bile acid, 3α, 7α, 12α, 26-tetrahydroxy-5β-cholest-23-en-27-oic acid
AU Yoshii, Michiko; Une, Mizuho; Kihira, Kenji; Kuramoto, Taiju; Akizawa, Toshifumi; Yoshioka, Masanori; Butler, Vincent P., Jr.; Hoshita, Takahiko
CS Sch. Med., Hiroshima Univ., Hiroshima, 734, Japan
SO Journal of Lipid Research (1994), 35(9), 1646-51
CODEN: JLPRAW; ISSN: 0022-2275
DT Journal
LA English
CC 6-5 (General Biochemistry)
AB The bile salts present in gallbladder bile of the toad, Bufo marinus, were found to consist of a mixture of bile alc. sulfates and **unconjugated** bile acids. The major bile alc. was 5β-bufol; 5α- and 5β-cholestane-3α, 7α, 12α, 26-tetrols occurred as the minor bile alcs. Bile acids of Bufo marinus were cholic acid, allocholic acid, 3α,7α,12α-trihydroxy-5α- and 5β-cholestan-26-oic acids, 3α,7α,12α-trihydroxy-5α- and 5β-cholest-23-en-26-oic acids, 3α,7a,12α,26-tetrahydroxy-5β-cholestan-27-oic acid, and a C27 bile acid which has not been previously described. By chromatog. behavior, mass spectral data, and identification of the products of catalytic hydrogenation and ozonolysis, the structure of the new higher bile acid was elucidated as 3α,7α,12α,26-tetrahydroxy-5β-cholest-23-en-27-oic acid. The bile salt pattern of Bufo marinus closely resembles that of Bufo vulgaris formosus, except for the absence of 3α,7α,12α-trihydroxy-5β-cholest-22-ene-24-carboxylic acid, the major bile acid of the later toad.
ST Bufo bile salt tetrahydroxycholestenoic acid
IT Bile
Bufo marinus
(bile acids and bile salts of Bufo marinus)
IT Bile acids
Bile salts
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(bile acids and bile salts of Bufo marinus)
IT 81-25-4, Cholic acid 547-98-8 862-52-2D, 5α-Cholestane-3α, 7α, 12α, 26-tetrol, sulfate esters 862-53-3D,

5β-Cholestane-3α, 7α, 12α, 26-tetrol, sulfate esters 2464-18-8 6127-75-9D, sulfate esters 17708-88-2, 3α,7α,12α-Trihydroxy-5α-cholestan-26-oic acid 73834-17-0 **84888-63-1 88498-08-2** 159330-16-2
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(bile acids and bile salts of Bufo marinus)

IT **84888-63-1 88498-08-2**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(bile acids and bile salts of Bufo marinus)

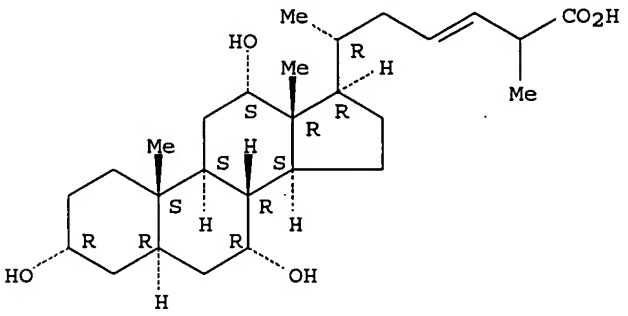
RN 84888-63-1 HCAPLUS
CN Cholest-23-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 88498-08-2 HCAPLUS
CN Cholest-23-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5α,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L40 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1994:686635** HCAPLUS
DN 121:286635
ED Entered STN: 10 Dec 1994
TI Compositions containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease
IN Sipos, Tibor
PA Digestive Care Inc., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent

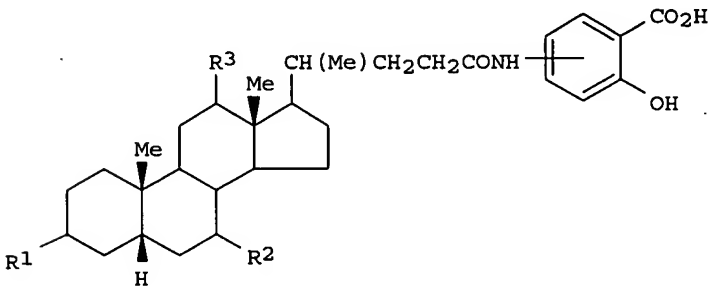
LA English
IC ICM A61K031-56
INCL 514182000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 26
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5352682	A	19941004	US 1993-27693	19930308 <--
PRAI US 1993-27693		19930308 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5352682	ICM	A61K031-56
	INCL	514182000
US 5352682	NCL	514/182.000; 424/451.000; 514/788.100; 552/553.000; 552/554.000
	ECLA	A61K031/60 <--

OS MARPAT 121:286635
GI



I

AB Disclosed are compns. containing bile acid-aminosalicylate **conjugates** I (R1 = OH in α or β position; R2 = OH; R3 = H, OH; R4 = H, acetyl) or a pharmaceutically acceptable salt thereof. Also disclosed are a process for preparing the **conjugates** and methods for treating/preventing gastrointestinal disorders, impaired liver function, etc. using the **conjugates**.

ST bile acid aminosalicylate **conjugate** prepn therapeutic; pharmaceutical bile acid aminosalicylate **conjugate**; deficiency disease bile acid aminosalicylate **conjugate**; antiinflammatory pharmaceutical bile acid aminosalicylate **conjugate**

IT Inflammation inhibitors
Pharmaceutical dosage forms
(compns..containing acid-aminosalicylate **conjugates** or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Therapeutics
(for bile acid deficiency disease; compns. containing acid-aminosalicylate **conjugates** or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT **Pharmaceutical dosage forms**
(caplets, compns. containing acid-aminosalicylate **conjugates** or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Bile acids
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**, with aminosalicylates; compns. containing acid-aminosalicylate **conjugates** or salts thereof for

treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolic disorders, deficiency, disease; compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Pharmaceutical dosage forms
(microspheres, compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT Pharmaceutical dosage forms
(microtablets, compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 28088-64-4DP, Aminosalicylic acid, bile acid conjugates
159026-16-1P 159026-17-2P 159026-20-7P
159026-23-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 159026-15-0 159026-18-3 159026-19-4
159026-21-8 159026-22-9 159026-24-1
159026-25-2 159026-26-3 159026-27-4
159026-28-5 159026-29-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

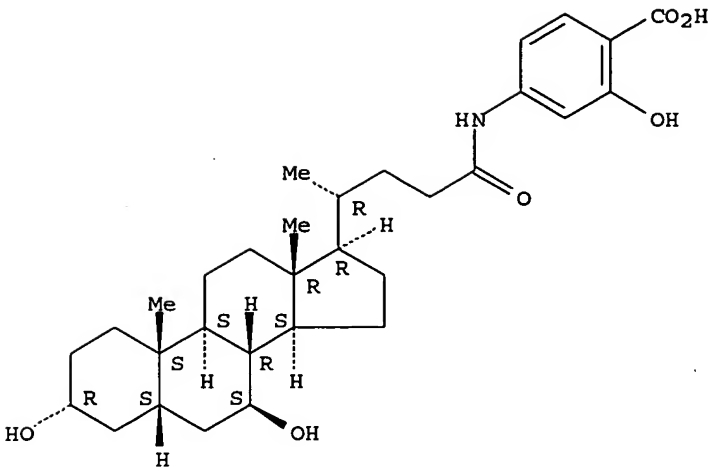
IT 37289-07-9, Cholylglycine hydrolase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease in relation to conjugate hydrolysis)

IT 65-49-6, 4-Aminosalicylic acid 81-25-4, Cholic acid 89-57-6, 5-Aminosalicylic acid 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of and compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

IT 159026-16-1P 159026-17-2P 159026-20-7P
159026-23-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)

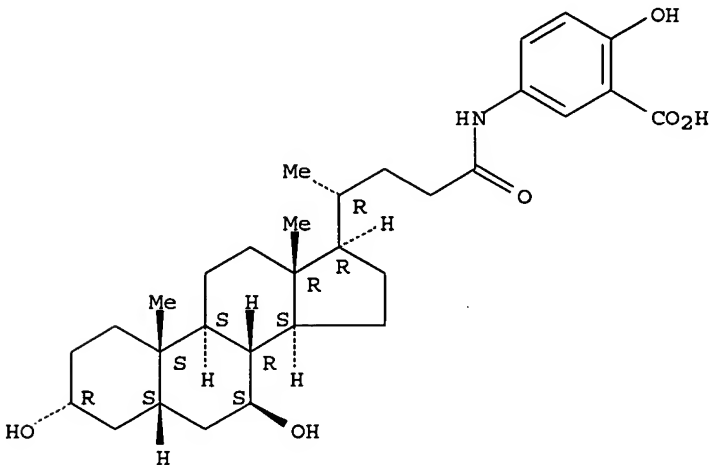
RN 159026-16-1 HCAPLUS
CN Benzoic acid, 4-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



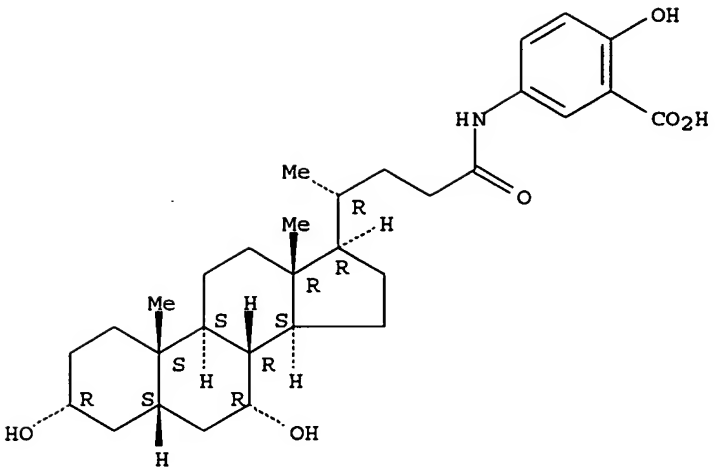
RN 159026-17-2 HCAPLUS
CN Benzoic acid, 5-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



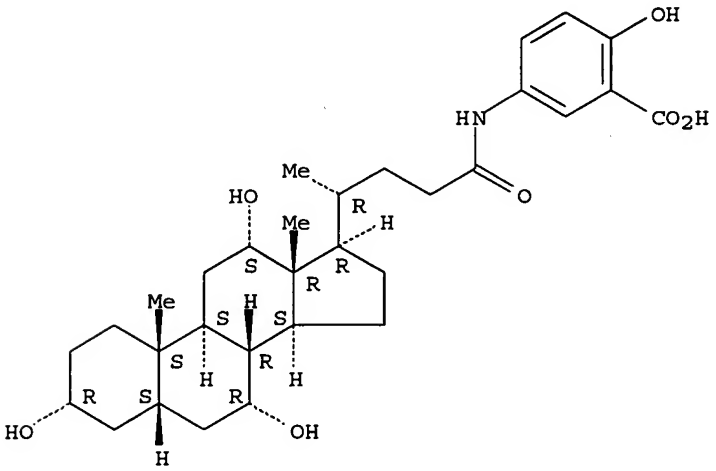
RN 159026-20-7 HCAPLUS
CN Benzoic acid, 5-[[(3α,5β,7α)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



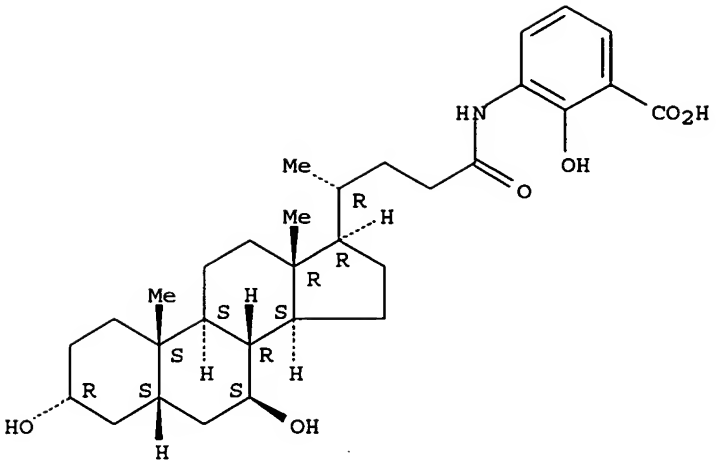
RN 159026-23-0 HCAPLUS
CN Benzoic acid, 2-hydroxy-5-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



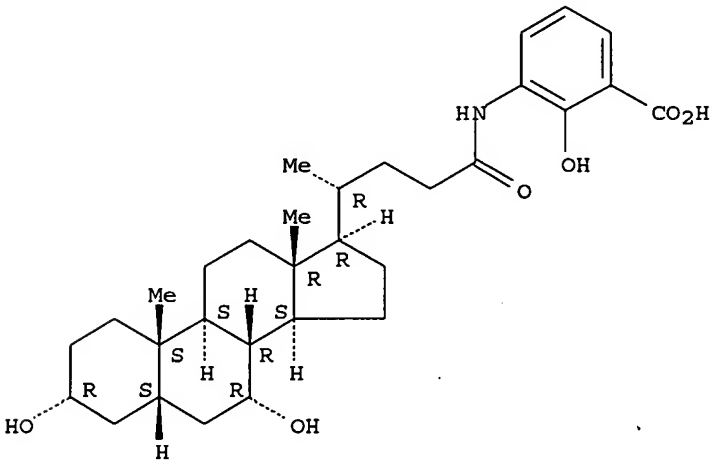
IT **159026-15-0 159026-18-3 159026-19-4**
159026-21-8 159026-22-9 159026-24-1
159026-25-2 159026-26-3 159026-27-4
159026-28-5 159026-29-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing acid-aminosalicylate **conjugates** or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)
RN 159026-15-0 HCAPLUS
CN Benzoic acid, 3-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



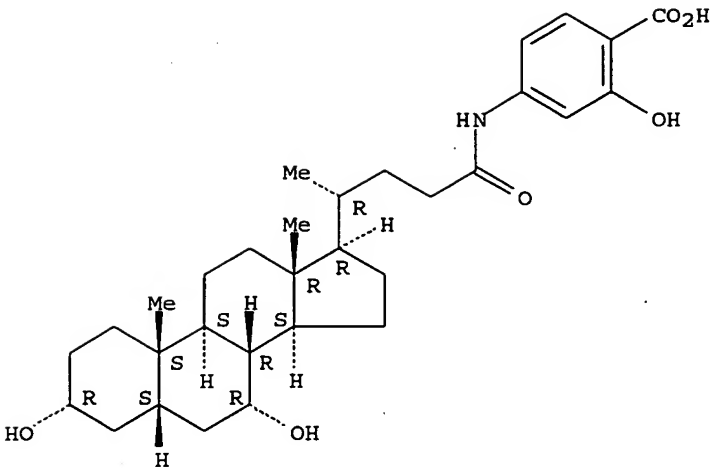
RN 159026-18-3 HCAPLUS
CN Benzoic acid, 3-[[(3α,5β,7α)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



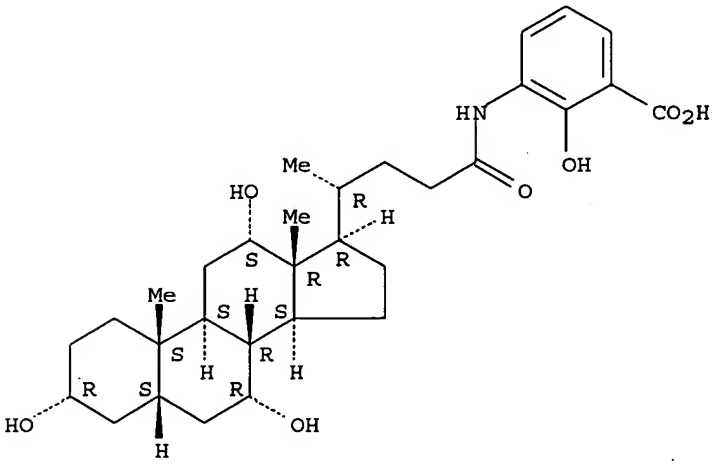
RN 159026-19-4 HCAPLUS
CN Benzoic acid, 4-[[(3α,5β,7α)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



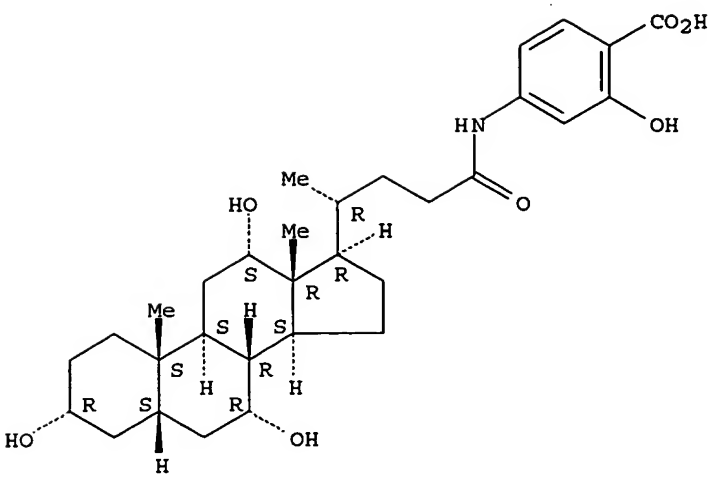
RN 159026-21-8 HCAPLUS
CN Benzoic acid, 2-hydroxy-3-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



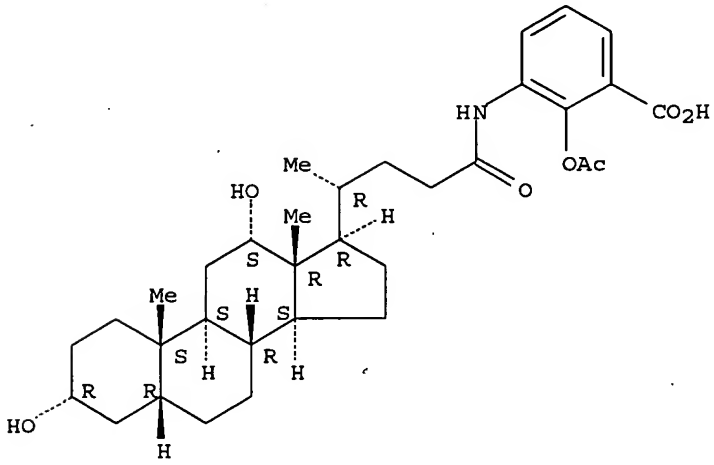
RN 159026-22-9 HCAPLUS
CN Benzoic acid, 2-hydroxy-4-[[(3α,5β,7α,12α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



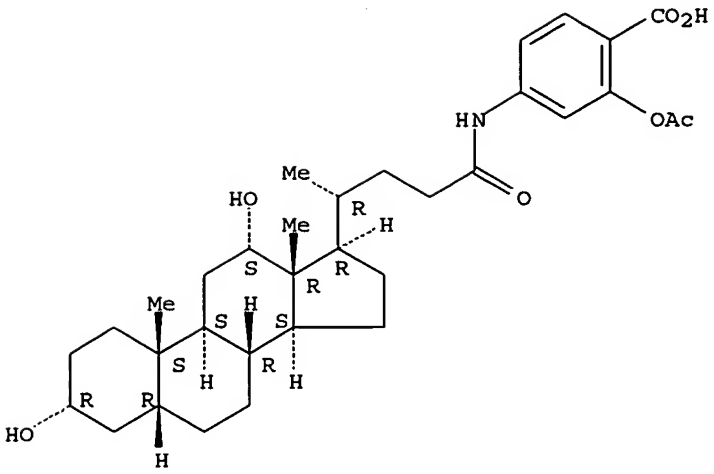
RN 159026-24-1 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)-3-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



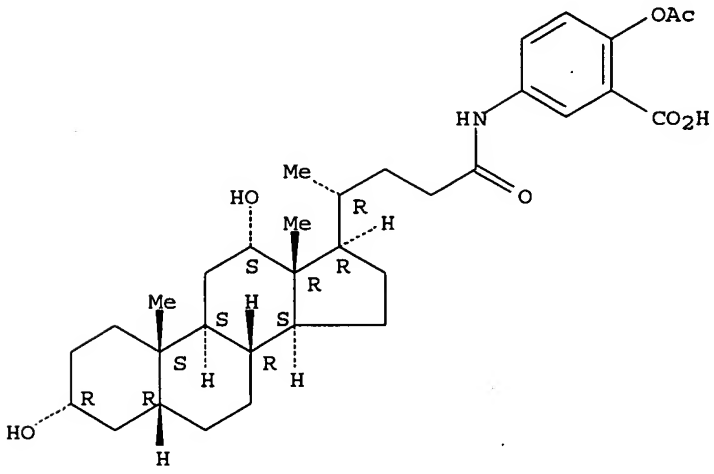
RN 159026-25-2 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)-4-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159026-26-3 HCAPLUS
CN Benzoic acid, 2-(acetyloxy)-5-[[(3α,5β,12α)-3,12-dihydroxy-24-oxocholan-24-yl]amino]- (9CI) (CA INDEX NAME)

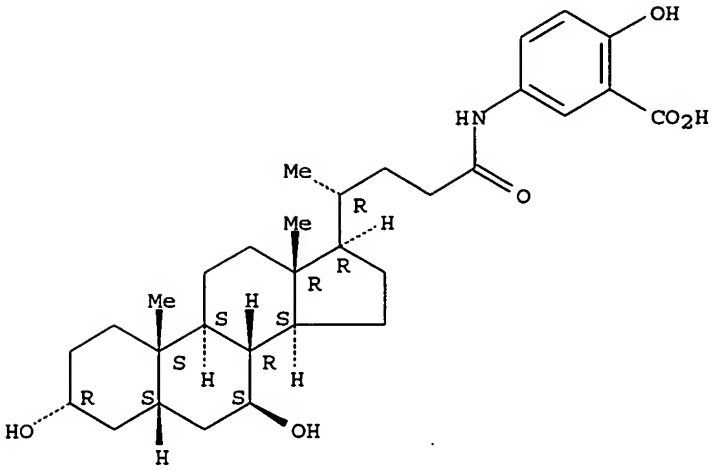
Absolute stereochemistry.



RN 159026-27-4 HCAPLUS
CN Benzoic acid, 5-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, sodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



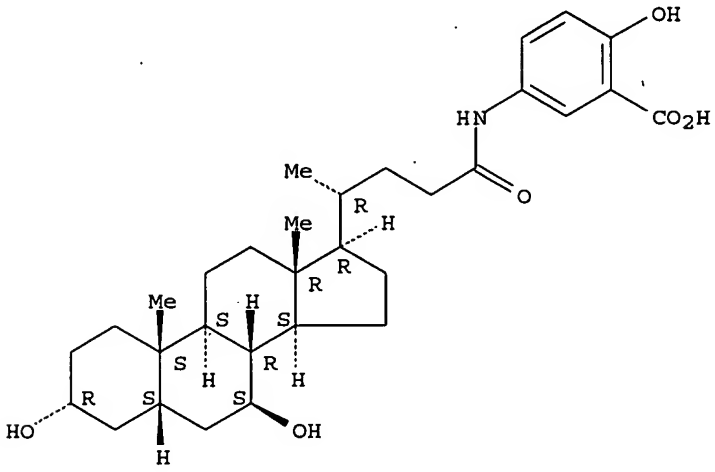
PAGE 2-A

●x Na

RN 159026-28-5 HCAPLUS
CN Benzoic acid, 5-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, potassium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

●x K

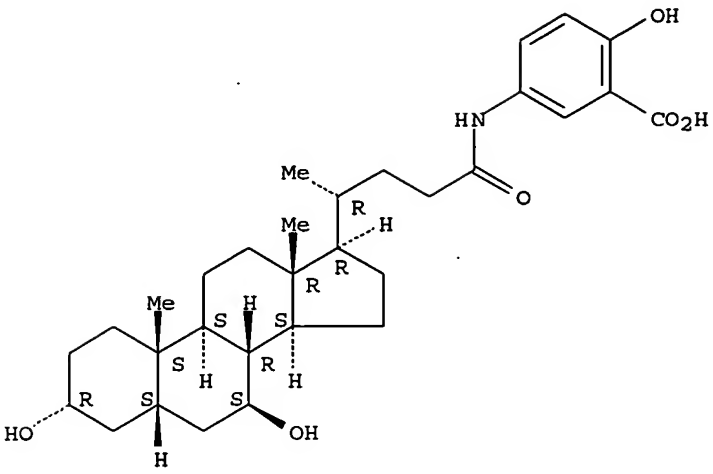
RN 159026-29-6 HCAPLUS
CN Benzoic acid, 5-[[(3α,5β,7β)-3,7-dihydroxy-24-oxocholan-24-yl]amino]-2-hydroxy-, compd. with 2-amino-2-(hydroxymethyl)-1,3-

propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

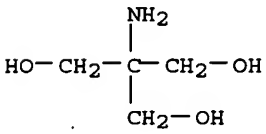
CRN 159026-17-2
CMF C31 H45 N O6

Absolute stereochemistry.



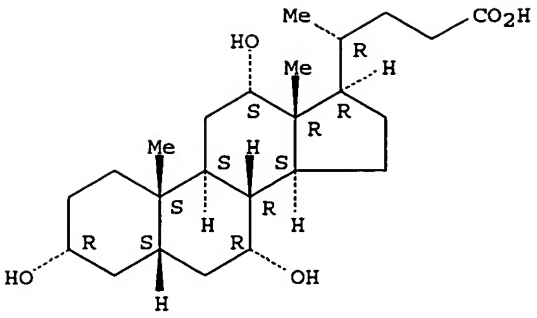
CM 2

CRN 77-86-1
CMF C4 H11 N O3



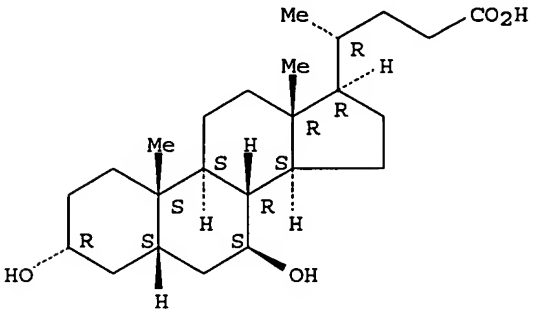
IT 81-25-4, Cholic acid 128-13-2, Ursodeoxycholic acid
474-25-9, Chenodeoxycholic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of and compns. containing acid-aminosalicylate conjugates or salts thereof for treating/preventing a bile acid deficiency condition and inflammatory disease)
RN 81-25-4 HCAPLUS
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



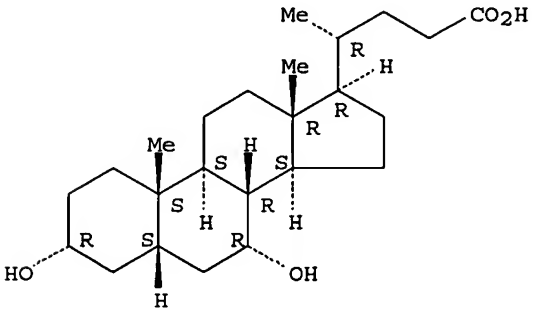
RN 128-13-2 HCAPLUS
CN Cholan-24-oic acid, 3,7-dihydroxy-, (3α,5β,7β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 474-25-9 HCAPLUS
CN Cholan-24-oic acid, 3,7-dihydroxy-, (3α,5β,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:173477 HCAPLUS
DN 120:173477
ED Entered STN: 02 Apr 1994
TI The use of nor- and homo- bile acid derivatives as absorption enhancers for medicaments
IN Berlati, Fabio; Ceschel, Giancarlo; Roda, Aldo; Roda, Enrico; Ronchi, Celestino
PA Monteresearch S.r.l., Italy
SO PCT Int. Appl., 14 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-28
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9400155	A1	19940106	WO 1993-EP1508	19930615	<--
	W: JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	EP 652773	A1	19950517	EP 1993-912975	19930615	<--
	EP 652773	B1	19980107			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 07508013	T2	19950907	JP 1993-501998	19930615	<--
	AT 161731	E	19980115	AT 1993-912975	19930615	<--
	ES 2114056	T3	19980516	ES 1993-912975	19930615	<--
	US 5656277	A	19970812	US 1994-360833	19941228	<--
PRAI	IT 1992-MI1601	A	19920630	<--		
	WO 1993-EP1508	W	19930615	<--		

CLASS

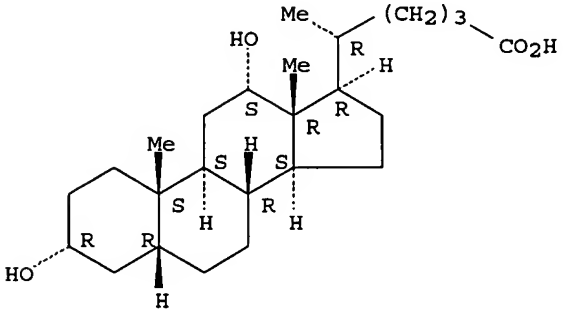
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9400155	ICM	A61K047-28
US 5656277	NCL	424/400.000; 424/435.000; 424/436.000; 424/451.000; 424/464.000; 424/489.000; 514/169.000; 514/171.000; 514/182.000; 514/553.000; 514/569.000
	ECLA	A61K047/28 <--

AB Nor- and homo- bile acid derivs. and their **conjugates** with taurine, glycine, and alanine in C23 and C25 are used as absorption enhancers for medicaments administered by the enteral route or by other routes, such as intranasal, buccal and sublingual routes. The derivs. improve the absorption of medicaments through mucosa without being metabolized by the intestinal flora, thus allowing a fast excretion. Moreover, the derivs. have a negligible toxicity. For example, a suppository contained Na diclofenac 0.1, homochenodeoxycholic acid 0.02, and Witepsol H-15 2.5g.

ST bile acid drug absorption enhancer; norbile acid drug absorption enhancer
IT Bile acids
RL: BIOL (Biological study)
(as absorption enhancers for drugs)
IT Antihistaminics
Cardiovascular agents
Cholinergic antagonists
Diuretics
Inflammation inhibitors
Hormones
Steroids, biological studies
RL: BIOL (Biological study)
(dosage forms of, bile acid derivs. as absorption enhancers in)
IT Peptides, biological studies
RL: BIOL (Biological study)
(drugs, dosage forms of, bile acid derivs. as absorption enhancers in)
IT **Pharmaceutical dosage forms**
(buccal, bile acid derivs. as absorption enhancers in)
IT Bile acids
RL: BIOL (Biological study)
(**conjugates**, with taurine and glycine and alanine, as absorption enhancers for drugs)
IT Anesthetics
(local, dosage forms of, bile acid derivs. as absorption enhancers in)
IT **Pharmaceutical dosage forms**
(**nasal**, bile acid derivs. as absorption enhancers in)
IT Bile acids
RL: BIOL (Biological study)
(nor-, 3,7-dihydroxy, as absorption enhancers for drugs)

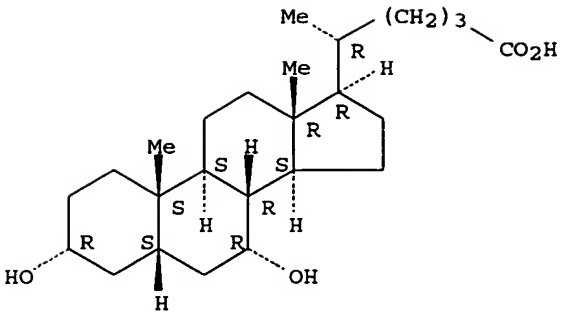
IT **Pharmaceutical dosage forms**
(**suppositories**, bile acid derivs. as absorption enhancers in)
IT **Pharmaceutical dosage forms**
(**tablets**, bile acid derivs. as absorption enhancers in)
IT **38636-77-0 38636-78-1D**, Homochenodeoxycholic acid, **conjugates 53608-86-9**, Nordeoxycholic acid **86386-61-0**, Norchenodeoxycholic acid **99697-24-2**, Norursodeoxycholic acid **102044-28-0 153311-78-5 153311-79-6 153311-80-9 153481-25-5**
RL: BIOL (Biological study)
(as absorption enhancer for drugs)
IT **56-40-6D**, Glycine, **conjugates** with bile acids **56-41-7D**, Alanine, **conjugates** with bile acids **107-35-7D**, Taurine, **conjugates** with bile acids
RL: BIOL (Biological study)
(as absorption enhancers for drugs)
IT **9034-40-6**, LHRH
RL: BIOL (Biological study)
(buccal dosage forms containing, bile acid derivs. as absorption enhancers in)
IT **9007-12-9**, Calcitonin
RL: BIOL (Biological study)
(rectal capsules containing, bile acid derivs. as absorption enhancers in)
IT **15307-79-6**, Sodium diclofenac
RL: BIOL (Biological study)
(suppository containing, bile acid derivs. as absorption enhancers in)
IT **54-31-9**, Furosemide **68-89-3**, Dipyrone **443-48-1**, Metronidazole
RL: BIOL (Biological study)
(tablets containing, bile acid derivs. as absorption enhancers in)
IT **38636-77-0 38636-78-1D**, Homochenodeoxycholic acid, **conjugates 53608-86-9**, Nordeoxycholic acid **86386-61-0**, Norchenodeoxycholic acid **99697-24-2**, Norursodeoxycholic acid **102044-28-0 153311-78-5 153311-80-9**
RL: BIOL (Biological study)
(as absorption enhancer for drugs)
RN 38636-77-0 HCAPLUS
CN Cholane-24-carboxylic acid, 3,12-dihydroxy-, (3α,5β,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



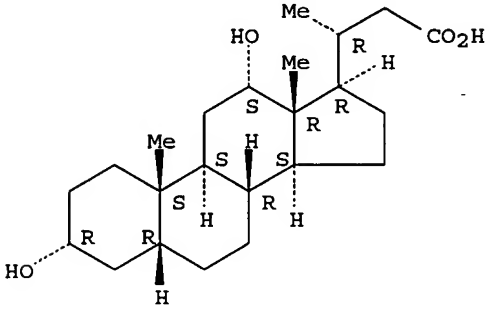
RN 38636-78-1 HCAPLUS
CN Cholane-24-carboxylic acid, 3,7-dihydroxy-, (3α,5β,7α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



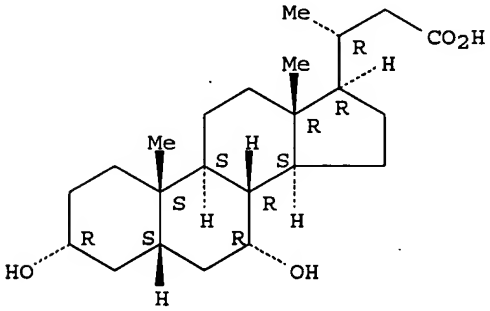
RN 53608-86-9 HCAPLUS
CN 24-Norcholan-23-oic acid, 3,12-dihydroxy-, (3α,5β,12α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



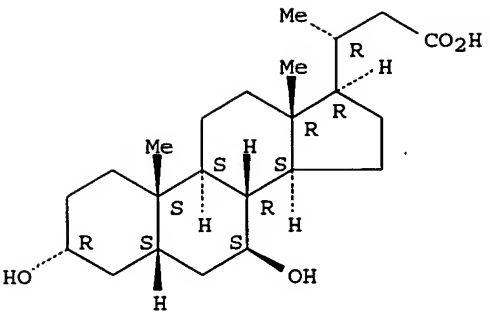
RN 86386-61-0 HCAPLUS
CN 24-Norcholan-23-oic acid, 3,7-dihydroxy-, (3α,5β,7α)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



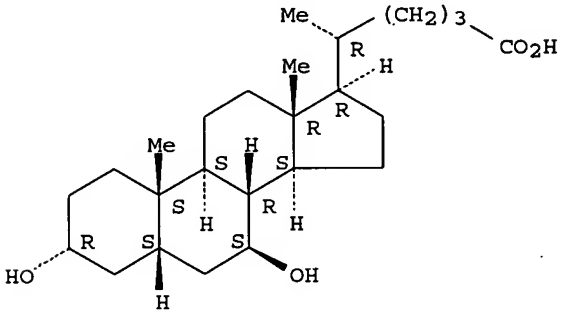
RN 99697-24-2 HCAPLUS
CN 24-Norcholan-23-oic acid, 3,7-dihydroxy-, (3α,5β,7β)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



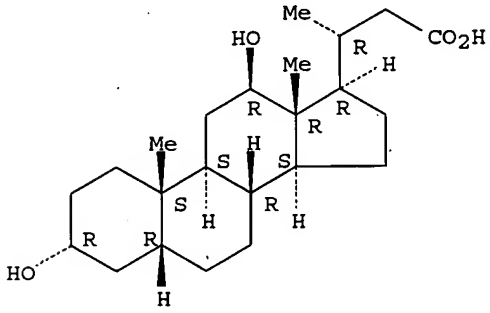
RN 102044-28-0 HCAPLUS
CN Cholane-24-carboxylic acid, 3,7-dihydroxy-, (3α,5β,7β)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



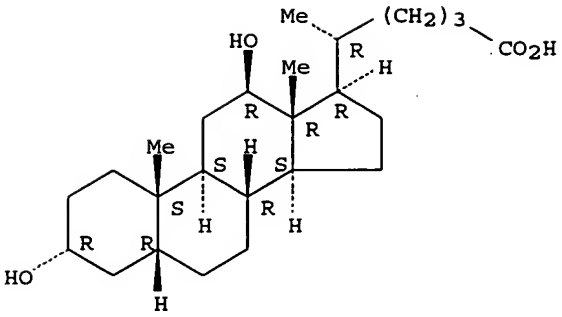
RN 153311-78-5 HCAPLUS
CN 24-Norcholan-23-oic acid, 3,12-dihydroxy-, (3α,5β,12β)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153311-80-9 HCAPLUS
CN Cholane-24-carboxylic acid, 3,12-dihydroxy-, (3α,5β,12β)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L40 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:546478 HCAPLUS
DN 117:146478
ED Entered STN: 17 Oct 1992
TI Bile acids and **conjugates** identified in metabolic disorders by fast atom bombardment and tandem mass spectrometry
AU Libert, Raymond; Hermans, Dominique; Draye, Jean Pierre; Van Hoof, Francois; Sokal, Etienne; De Hoffmann, Edmond
CS Dep. Neuropediatry, Clin. Univ. St. Luc, Brussels, B-1200, Belg.
SO Clinical Chemistry (Washington, DC, United States) (1991), 37(12), 2102-10
CODEN: CLCHAU; ISSN: 0009-9147
DT Journal
LA English
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 14, 73, 80
AB From a study of the collision-activated fragmentation of bile acids, a qual. anal. method based on neg.-ion fast-atom-bombardment (FAB) tandem mass spectrometry was developed. The times for sample preparation and analyses are short. Both free and **conjugated** bile acids are detected as they occur in biol. fluids, acids are detected as they occur in biol. fluids, without derivatization. For identifying bile acids and **conjugates**, the method offers better specificity and sensitivity than does the fast atom bombardment mass spectrometric technique alone. Specific scan modes were developed for the selective detection of taurine **conjugates**, Δ4-unsatd. taurine **conjugates**, Δ4-3-keto free acids and their glycine **conjugates**, free acids and glycine **conjugates** bearing a hydroxyl group at the C-12 position, sulfates of glycine and taurine **conjugates**, and a C29 dicarboxylic bile acid, specific for generalized peroxisomal disorders. Applications of this technique demonstrate its potential usefulness, principally in the diagnosis of several peroxisomal disorders.
ST body fluid bile acid **conjugate** detection; peroxisome disorder diagnosis bile acid; mass spectrometry bile acid diagnosis
IT Bile
Blood analysis
Urine analysis
(bile acids and their **conjugates** detection in human, by fast-atom-bombardment and tandem mass spectrometry)
IT Body fluid
(bile acids and their **conjugates** detections in, by fast-atom-bombardment and tandem mass spectrometry)
IT Bile acids
Bile salts
RL: ANT (Analyte); ANST (Analytical study)
(detection of, in biol. fluids by fast-atom-bombardment tandem mass spectrometry, in metabolic disorder diagnosis)
IT Mass spectra
(of bile acids and their **conjugates**)
IT Bile acids

RL: ANT (Analyte); ANST (Analytical study)
(conjugates, detection of, in biol. fluids by fast-atom-bombardment tandem mass spectrometry, in metabolic disorder diagnosis)

IT Peroxisome
(disease, diagnosis of, bile acid detection in body fluids by mass spectrometry in)

IT Animal metabolism
(disorder, diagnosis of, bile acid detection in human body fluid by mass spectrometry in)

IT Bile acids
RL: ANT (Analyte); ANST (Analytical study)
(sulfates, detection of, in biol. fluids by fast-atom-bombardment tandem mass spectrometry, in metabolic disorder diagnosis)

IT 516-35-8 640-79-9 13587-11-6 117590-83-7 129944-49-6 143380-61-4 143380-62-5 143380-63-6 **143442-55-1** 143476-63-5 143477-50-3
RL: ANT (Analyte); ANST (Analytical study)
(detection of, in biol. fluid by mass spectrometry)

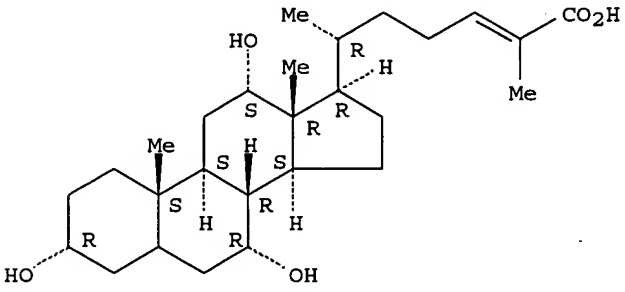
IT 56-40-6, Glycine, analysis 81-24-3, Taurocholic acid 81-25-4 108-88-3D, Toluene, bile acid conjugates 474-25-9 475-31-0, Glycocholic acid 68714-85-2 68756-88-7 117590-89-3 129944-53-2 143380-64-7 143384-75-2 143442-56-2 143442-57-3 143476-45-3 143476-62-4
RL: ANT (Analyte); ANST (Analytical study)
(detection of, in biol. fluids by mass spectrometry)

IT 60-18-4, L-Tyrosine, analysis
RL: ANST (Analytical study)
(metabolic disorders, tyrosine of, type 1, diagnosis of, by bile acid mass spectrometry)

IT **143442-55-1**
RL: ANT (Analyte); ANST (Analytical study)
(detection of, in biol. fluid by mass spectrometry)

RN 143442-55-1 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L40 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:421765 HCAPLUS
DN 113:21765
ED Entered STN: 21 Jul 1990
TI Bile acid profiles in peroxisomal 3-oxoacyl-coenzyme A thiolase deficiency
AU Clayton, Peter T.; Patel, Ella; Lawson, Alexander M.; Carruthers, Robert A.; Collins, Janna
CS Dep. Child Health, Inst. Child Health, London, WC1N 1EH, UK
SO Journal of Clinical Investigation (1990), 85(4), 1267-73
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English

CC 14-14 (Mammalian Pathological Biochemistry)

AB Fast atom bombardment mass spectrometry and gas chromatog.-mass spectrometry were used to analyze bile acids in the body fluids of an infant (L.C.) whose liver contained no immunoreactive peroxisomal 3-oxoacyl-CoA thiolase. The profiles were compared with those of six patients with undetectable peroxisomes (Zellweger syndrome) and two siblings (N.B. and I.B.) whose defect of peroxisomal β-oxidation could not be localized by morphol. studies of peroxisomes or by immunoblotting of peroxisomal β-oxidation proteins. 3α,7α,12α-Trihydroxy-5β-cholestan-26-oic acid (THCA) was present in bile and plasma of all patients. However, bile from L.C., N.B. and I.B. contained unconjugated varanic acid (3α,7α,12α,24-tetrahydroxy-5β-cholestan-26-oic acid) as the major C27 bile acid, whereas bile from Zellweger patients contained only small amts. of varanic acid. In the bile from L.C. two isomers of varanic acid were present; in the bile from N.B. and I.B. a single isomer predominated. L.C., N.B., and I.B. all produced bile containing small amts. of (24E)-3α,7α,12α-trihydroxy-5β-cholest-24-en-26-oic acid ([24E]-Δ24-THCA), its [24Z]-isomer, 3α,7α,12α-trihydroxy-5β-cholest-23-en-26-oic acid and 3α,7α,12α-trihydroxy-27-nor-5β-cholestan-24-one. The results provide evidence for peroxisomal pathways for cholic acid synthesis in man via THCA, Δ24-THCA, and varanic acid and show that bile acid analyses can be used to diagnose peroxisomal thiolase deficiency.

ST bile acid profile oxoacylCoA thiolase deficiency

IT Blood plasma
Urine
(bile acid profiles of, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT Body fluid
(duodenal, bile acid profiles of, in diagnosis of peroxisomal oxoacyl-CoA thiolase deficiency of humans)

IT Bile acids
RL: BIOL (Biological study)
(of body fluids, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT Peroxisome
(oxoacyl-CoA thiolase deficiency of, bile acid profiles of body fluids in diagnosis of, of humans)

IT 9029-97-4, 3-Oxoacyl-CoA thiolase
RL: BIOL (Biological study)
(deficiency of, bile acid profiles of duodenal juice in diagnosis of, of humans)

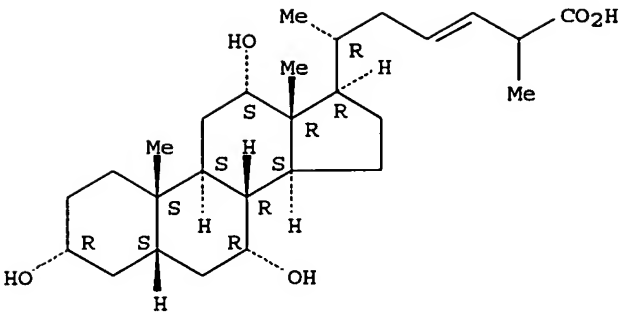
IT 81-25-4, Cholic acid 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid 547-98-8 1061-64-9 61628-32-8 72883-89-7 73834-17-0 **84888-63-1** **85552-38-1** **85552-39-2** 85552-42-7
RL: BIOL (Biological study)
(of duodenal juice, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

IT **84888-63-1** **85552-38-1** **85552-39-2**
RL: BIOL (Biological study)
(of duodenal juice, in peroxisomal oxoacyl-CoA thiolase deficiency of humans, diagnosis in relation to)

RN 84888-63-1 HCAPLUS

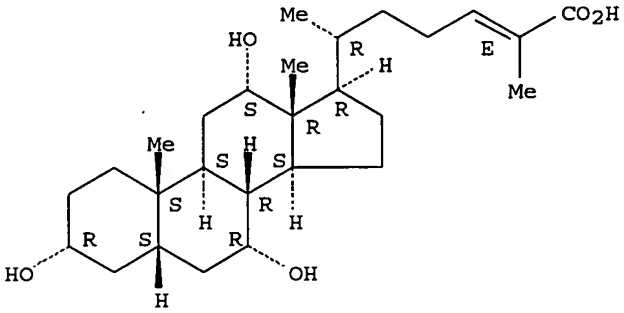
CN Cholest-23-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



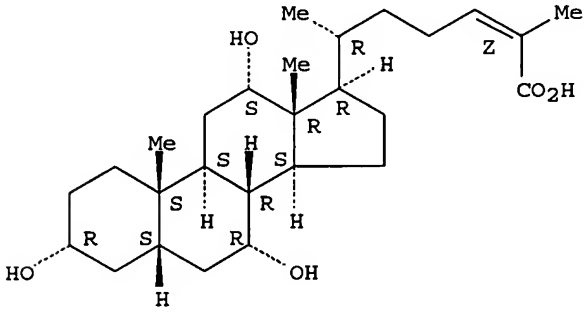
RN 85552-38-1 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α,24E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



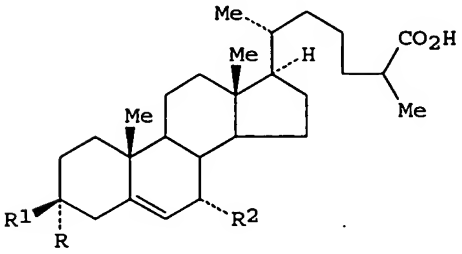
RN 85552-39-2 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L40 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:471021 HCAPLUS
DN 109:71021
ED Entered STN: 02 Sep 1988
TI Occurrence of 3β-hydroxy-5-cholestenoic acid, 3β,7α-dihydroxy-5-cholestenoic acid, and 7α-hydroxy-3-oxo-4-cholestenoic acid as normal constituents in human blood
AU Axelson, Magnus; Moerk, Birgitta; Sjoevall, Jan

CS Dep. Clin. Chem., Karolinska Hosp., Stockholm, 104 01, Swed.
SO Journal of Lipid Research (1988), 29(5), 629-41
CODEN: JLPRAW; ISSN: 0022-2275
DT Journal
LA English
CC 13-5 (Mammalian Biochemistry)
GI



I, R=R2=H, R1=OH
II, R=H, R1=R2=OH
III, RR1=O, R2=OH

AB Three unconjugated C27 bile acids were found in plasma from healthy humans. They were isolated by liquid-solid extraction and anion-exchange chromatog. and were identified by gas-liquid chromatog.-mass spectrometry, microchem. reactions, and UV spectroscopy as 3β-hydroxy-5-cholestenoic, 3β,7α-dihydroxy-5-cholestenoic, and 7α-hydroxy-3-oxo-4-cholestenoic acids (I, II, and III, resp.). Their levels often exceeded those of the unconjugated C24 bile acids and the variations between individuals were smaller than for the C24 acids. The concns. in plasma from healthy subjects were 67.2 ng/mL for I, 38.9 ng/mL for II, and 81.7 ng/mL for III. The levels of the individual acids were pos. correlated with each other and not with the levels of the C24 acids. The cholestenoic acids were below the detection limit (20-50 ng/mL) in bile, and C27 bile acids present in bile were not detected in plasma.

ST cholestenoic acid deriv blood plasma; bile acid C27 blood plasma

IT Feeding
(bile acids of blood plasma of human response to)

IT Bile
Blood plasma
(bile acids of, of human)

IT Bile acids
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of bile, of human, bile acids of blood plasma in relation to)

IT Bile acids
RL: BIOL (Biological study)
(of blood plasma of human)

IT 81-25-4, Cholic acid 474-25-9, Chenodeoxycholic acid 547-98-8 5226-26-6 60696-62-0, Norcholic acid 72883-89-7 73804-37-2 73834-17-0, 3α,7α,12α,26-Tetrahydroxy-5β-cholestan-27-oic acid 73837-07-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of bile, of human)

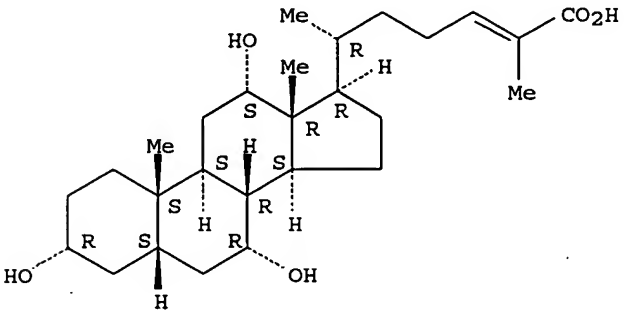
IT 6561-58-6 115538-84-6 115538-85-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of blood plasma, of human)

IT 115567-29-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidation of)

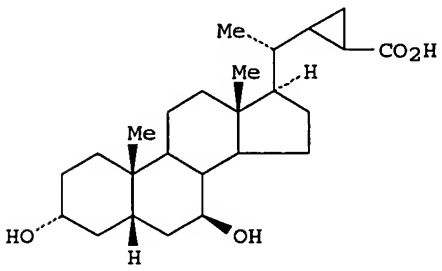
IT 115538-86-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 5226-26-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of bile, of human)
RN 5226-26-6 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L40 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:187048 HCAPLUS
DN 108:187048
ED Entered STN: 28 May 1988
TI Bile acids with a cyclopropyl-containing side chain. 3. Separation, identification, and properties of all four stereoisomers of 3α,7β-dihydroxy-22,23-methylene-5β-cholan-24-oic acid
AU Pellicciari, Roberto; Natalini, Benedetto; Cecchetti, Sergio; Porter, Barry; Roda, Aldo; Grigolo, Brunella; Balducci, Renzo
CS Ist. Chim. Farm. Tec. Farm., Univ. Studi, Perugia, 06100, Italy
SO Journal of Medicinal Chemistry (1988), 31(4), 730-6
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 32-6 (Steroids)
OS CASREACT 108:187048
GI



I

AB The 22,23-methylene-5β-cholan-24-oic acid I (CUDCA), a side-chain cyclopropylog of ursodeoxycholic acid (UDCA), was shown to be a mixture of four stereoisomers (CUDCA A-D). The 22S,23S, 22R,23R, 22S,23R, and 22R,23S diastereoisomers were separated, their resp. configurations assigned by 13C NMR spectroscopy, and original synthetic schemes for their preparation elaborated. Theor. models of the structure of UDCA and CUDCA A-D were built by using mol. computer graphic techniques. The four diastereoisomers greatly differ in hydrophilicity, in critical micellar

concentration in water, and exhibit a different interaction with intestinal bacterial enzymes. CUDCA A-C are not conjugated with glycine or taurine in the liver, while CUDCA D is secreted into bile predominantly as taurine and glycine conjugate.

ST methylenecholanoic acid stereoisomer configuration; cholanic acid methylene stereoisomer configuration; bile acid biol activity diastereoisomer

IT Molecular structure-biological activity relationship
(of 3α,7β-dihydroxy-22,23-methylene-5β-cholan-24-oic acid diastereomers)

IT 105360-63-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclopropanation of, with Et diazoacetate)

IT 128-13-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)

IT 113181-05-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetylation of)

IT 113218-62-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and addition reaction with Et diazoacetate)

IT 113181-08-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and attempted cyclopropanation of)

IT 113299-41-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion into acetylene derivative)

IT 113181-06-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cyclopropanation with diazomethane)

IT 113181-04-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and elimination reaction of)

IT 113181-07-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)

IT 69519-36-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and phenylselenylation of)

IT 89414-90-4P 89495-32-9P 89495-33-0P 89495-34-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

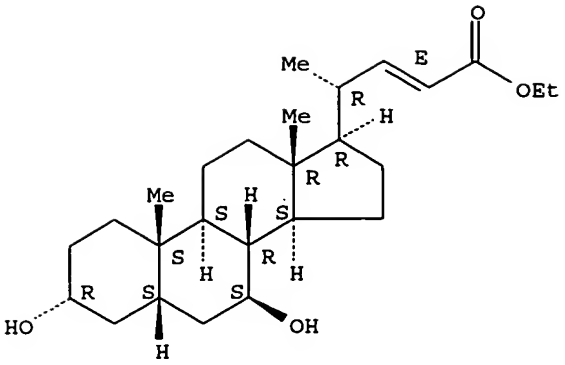
IT 91378-92-6P 91423-31-3P 91423-32-4P 91423-33-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, purification, configuration, and biol. activity of)

IT 113181-05-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetylation of)

RN 113181-05-8 HCAPLUS

CN Chol-22-en-24-oic acid, 3,7-dihydroxy-, ethyl ester, (3α,5β,7β,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L40 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:154139 HCAPLUS
DN 106:154139
ED Entered STN: 15 May 1987
TI Identification of **unconjugated** bile acids in human bile
AU Matoba, Naoyuki; Une, Mizuho; Hoshita, Takahiko
CS Fac. Med., Kyushu Univ., Maidashi, 3-1-1, Japan
SO Journal of Lipid Research (1986), 27(11), 1154-62
CODEN: JLPRAW; ISSN: 0022-2275
DT Journal
LA English
CC 14-7 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13
AB **Unconjugated** bile acids in the bile of healthy and diseased (cerebrotendinous xanthomatosis) humans were determined qual. and quant. by gas-liquid chromatog. and gas-liquid chromatog.-mass spectrometry, after their isolation by ion-exchange chromatog. In a healthy person and 3 patients with cholelithiasis, **unconjugated** bile acids comprised 0.1-0.4% of total biliary bile acids. The bile acid composition of the **unconjugated** fraction was quite different from that of the glycine- or taurine-**conjugate** fraction, in that it contained a relatively large proportion of unusual bile acids including C23 and C27 bile acids. In 2 patients with cerebrotendinous xanthomatosis, C22 and C23 bile acids were the major constituents of the biliary **unconjugated** bile acids and comprised about 0.8% of total bile acids; no detectable amts. of C27 bile acids were found in their bile. The anal. of biliary **unconjugated** bile acids may be useful for the diagnosis of metabolic diseases concerning bile acids, particularly those diseases which involve the accumulation or disappearance of unusual bile acids.
ST bile acid bile cholelithiasis cerebrotendinous xanthomatosis
IT Calculi, biliary
(**unconjugated** bile acids of bile in, in humans)
IT Bile
(**unconjugated** bile acids of, of humans)
IT Bile acids
RL: BIOL (Biological study)
(**unconjugated**, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)
IT Xanthomatosis
(cerebrotendinous, **unconjugated** bile acids of bile in, in humans)
IT 56-40-6, biological studies 107-35-7, Taurine
RL: BIOL (Biological study)
(bile acids **conjugated** with, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)
IT 81-25-4, Cholic acid 83-44-3, Deoxycholic acid 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid 547-98-8

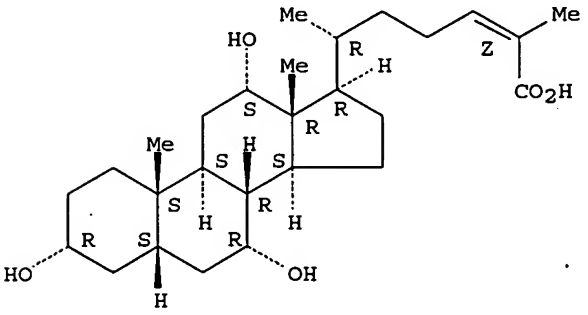
Search done by Noble Jarrell

911-40-0, 7-Ketodeoxycholic acid 2464-18-8, Allocholic acid 2955-27-3, 7-Epicholic acid 38917-20-3 60696-62-0, Norcholic acid 61844-74-4 73804-37-2 73834-17-0 73837-07-7 **85552-39-2** 86386-61-0 98349-18-9 99697-24-2 **107480-95-5**
RL: BIOL (Biological study)
(**unconjugated**, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)

IT **85552-39-2 107480-95-5**
RL: BIOL (Biological study)
(**unconjugated**, of bile in cerebrotendinous xanthomatosis and cholelithiasis and health in humans)

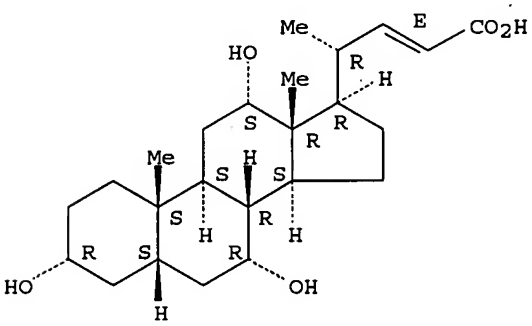
RN 85552-39-2 HCAPLUS
CN Cholest-24-en-26-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12α,24Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 107480-95-5 HCAPLUS
CN Chol-22-en-24-oic acid, 3,7,12-trihydroxy-, (3α,5β,7α,12.alpha.,22E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



=> b embase

FILE 'EMBASE' ENTERED AT 09:39:11 ON 24 JUN 2005

FILE COVERS 1974 TO 23 Jun 2005 (20050623/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all l48 tot

L48 ANSWER 1 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 2004197875 EMBASE
TI Absorption of the cholic acid-conjugated peptide hormone cholylsecretin from the rat ileum in vivo.
AU McHarg S.; Morton J.S.; McGinn B.J.; Yasin M.; **Morrison J.D.**
CS J.D. Morrison, West Medical Building, University of Glasgow, Glasgow G12 8QQ, United Kingdom
SO Acta Physiologica Scandinavica, (2004) Vol. 181, No. 1, pp. 23-34.
Refs: 29
ISSN: 0001-6772 CODEN: APSCAX
CY United Kingdom
DT Journal; Article
FS 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 20040610
Last Updated on STN: 20040610
AB Aims: Previously, we demonstrated that gastrin peptides as long as 34 amino acids were absorbed from the ileum of rat after conjugation to the C24 position of cholic acid and that these peptides retained full biological activity. As absorption was specific to the ileum, it was inferred that the conjugated hormone was taken up by the bile salt transporters. We have now extended these experiments to a member of a different family of hormones, viz. secretin, a 27-amino acid hormone that stimulates serous secretions from the exocrine pancreas. Methods: After conjugation to cholic acid, the degree of cholylsecretin absorption from the ileum of anaesthetized rats was assessed from the increase in pancreatic secretions. Results: A complication to the study was that intra-ileal infusion of native secretin caused a transient increase in the levels of pancreatic secretions. This was in contrast to the effects of intra-ileal infusion of cholylsecretin which did not cause this transient increase but, instead, gave rise to a delayed increase in pancreatic secretions which was sustained over several hours during which cholylsecretin was detected in plasma in high concentration by mass spectrometry. The pancreatic response to cholylsecretin was abolished by co-infusion of 50 mM taurocholate, employed to compete with the bile salt transporters, although a transient increase in pancreatic secretions similar to that caused by secretin was now generated. This was shown to arise from an action of taurocholate per se causing the release of endogenous secretin which is present in rat ileum. Conclusions: We, therefore, concluded that cholylsecretin had been absorbed from the rat ileum by uptake by bile salt transporters.
CT Medical Descriptors:
*hormone release
*hormonal regulation
*small intestine absorption
*ileum
drug effect
drug efficacy
drug mechanism
pancreas secretion
hormone blood level
secretin blood level
intestine absorption
pharmacological blocking
pancreas
nonhuman
male
rat

animal experiment
controlled study
animal tissue
article
priority journal
Drug Descriptors:
*cholic acid: PD, pharmacology
*secretin: EC, endogenous compound
*secretin: PD, pharmacology
recombinant hormone: PD, pharmacology
carrier protein: EC, endogenous compound
sodium chloride: EC, endogenous compound
taurocholic acid: PD, pharmacology
RN (cholic acid) **32500-01-9, 361-09-1, 81-25-4;**
(secretin) 1393-25-5, 17034-35-4, 73559-81-6; (carrier protein) 80700-39-6; (sodium chloride) 7647-14-5; (taurocholic acid) 145-42-6, 59005-70-8, 81-24-3
CO Sigma Aldrich

L48 ANSWER 2 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2002415967 EMBASE
TI Absorption of biologically active peptide hormones from the small intestine of rat.
AU **Wheeler S.**; McGinn B.J.; **Lucas M.L.**; **Morrison J.D.**
CS J.D. Morrison, West Medical Building, University of Glasgow, Glasgow G12 8QQ, United Kingdom
SO Acta Physiologica Scandinavica, (2002) Vol. 176, No. 3, pp. 203-213.
Refs: 34
ISSN: 0001-6772 CODEN: APSCAX
CY United Kingdom
DT Journal; Article
FS 002 Physiology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 20021202
Last Updated on STN: 20021202
AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anaesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amount of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each of the forms of gastrin was conjugated at the free amino terminus to the carboxyl group of cholic acid. Subsequent infusion of the conjugated form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addition, conjugation of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to intravenous injection of the hormone. Absorption of the gastrin conjugates was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.
CT Medical Descriptors:
*small intestine absorption
systemic circulation
acid secretion
ileum
stomach acid secretion
amino terminal sequence

conjugation
carboxy terminal sequence
drug effect
drug megadose
nonhuman
male
rat
animal experiment
controlled study
animal tissue
article
priority journal
Drug Descriptors:
*peptide hormone: DO, drug dose
*peptide hormone: PD, pharmacology
*peptide hormone: IV, intravenous drug administration
*gastrin: DO, drug dose
*gastrin: PD, pharmacology
*gastrin: IV, intravenous drug administration
cholic acid
RN (gastrin) 9002-76-0; (cholic acid) **32500-01-9, 361-09-1**
, 81-25-4

L48 ANSWER 3 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 91218502 EMBASE
DN 1991218502
TI The effect of sodium deoxycholate and other surfactants on the mucosal surface pH in proximal jejunum or rat.
AU McKie A.T.; Stewart W.; **Lucas M.L.**
CS Institute of Physiology, Glasgow University,Glasgow G12 8QQ, United Kingdom
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1991) Vol. 343, No. 6, pp. 659-664.
ISSN: 0028-1298 CODEN: NSAPCC
CY Germany
DT Journal; Article
FS 002 Physiology
004 Microbiology
029 Clinical Biochemistry
048 Gastroenterology
052 Toxicology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 911216
Last Updated on STN: 911216
AB The mucosal surface pH (acid microclimate) and nucleotide levels of rat proximal jejunum were measured in vivo under various conditions which included exposure to pharmacological agents and to surfactants. Mucosal surface pH was unaffected by sodium nitroprusside, A23187 and amiloride, as was mucosal cGMP content, although amiloride and A23187 reduced cAMP content. In contrast, surfactants elevated the pH of the mucosal surface significantly ($P < 0.001$): control value 6.23 ± 0.02 (n = 12); Lubrol PX 0.8% (v/v) 6.98 ± 0.02 (n = 5); sodium deoxycholate 2 mmol/l 6.67 ± 0.04 (n = 5); Triton X-100 0.5% (v/v) 7.41 ± 0.03 (n = 5). No significant changes in cGMP levels were noted after surfactant treatment, although DOC and Triton X-100 reduced cAMP levels. The ability of higher concentrations of surfactant to elevate the mucosal surface pH beyond neutrality to values similar to plasma pH contrasts with the action of Escherichia coli heat-stable (STa) enterotoxin which at high concentrations could not elevate the mucosal surface pH beyond neutrality. Consistent with the known effects on tight junction permeability, surfactants may act by allowing plasma-like subepithelial fluid to neutralise the microclimate.

CT Medical Descriptors:
*cell surface
*jejunum mucosa
*ph
animal experiment
animal tissue
article
controlled study
male
microscopy
nonhuman
priority journal
radioimmunoassay
rat
regional perfusion
Drug Descriptors:
*amiloride: PD, pharmacology
*calcimycin: PD, pharmacology
*cyclic gmp: EC, endogenous compound
*deoxycholate sodium: TO, drug toxicity
*nitroprusside sodium: PD, pharmacology
*surfactant: TO, drug toxicity
cyclic amp: EC, endogenous compound
docusate sodium: TO, drug toxicity
escherichia coli enterotoxin: TO, drug toxicity
lubrol: TO, drug toxicity
triton x 100: TO, drug toxicity
RN (amiloride) 2016-88-8, 2609-46-3; (calcimycin) 52665-69-7; (cyclic gmp) 7665-99-8; (deoxycholate sodium) 302-95-4; (nitroprusside sodium) 14402-89-2, 15078-28-1; (cyclic amp) 60-92-4; (docusate sodium) 577-11-7; (lubrol) 11138-41-3, 52434-01-2
CN Lubrol px; Triton x 100; A 23187

L48 ANSWER 4 OF 4 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 83183463 EMBASE
DN 1983183463
TI The effect of deoxycholate on intestinal surface pH and 5-methyltetrahydropteroylglutamate absorption in the rat proximal jejunum in vitro.
AU Blair J.A.; Hilburn M.E.; Lucas M.L.; Said H.M.
CS Dep. Chem., Univ. Aston Birmingham, Birmingham B4 7ET, United Kingdom
SO Biochemical Society Transactions, (1983) Vol. 11, No. 2, pp. 165-167.
CODEN: BCSTB5
CY United Kingdom
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
002 Physiology
048 Gastroenterology
LA English
ED Entered STN: 911209
Last Updated on STN: 911209
CT Medical Descriptors:
*5 methyltetrahydrofolic acid c 14
*drug absorption
*intestine absorption
*intestine mucosa
*ph
jejunum
nonhuman
rat
small intestine
animal cell
digestive system
Drug Descriptors:

*5 methyltetrahydrofolic acid
*deoxycholic acid
radioisotope
RN (5 methyltetrahydrofolic acid) 134-35-0; (deoxycholic acid) 83-44-3

=> d all l51 tot

L51 ANSWER 1 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 1999324376 EMBASE
TI Study of the pharmacological effect of the bile salt, sodium scymnol sulfate, from Rhizoprionodon acutus. IV. Effects of naturally occurring bile alcohols, bile acids and their conjugates on lesion development and vascular endothelial cell injury in a rat peripheral arterial occlusion model.
AU Ishida H.; Nakayasu H.; Tsuji K.
CS H. Ishida, School of Pharmaceutical Science, University of Shizuoka, 52-1 Yada, Shizuoka 422-8526, Japan
SO Biological and Pharmaceutical Bulletin, (1999) Vol. 22, No. 8, pp. 828-835.
Refs: 48
ISSN: 0918-6158 CODEN: BPBLEO
CY Japan
DT Journal; Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 19990930
Last Updated on STN: 19990930
AB A series of naturally occurring bile alcohols, bile acids and their conjugates has been investigated as part of our studies to develop unique anticoagulants with a potent prophylactic effect against vascular endothelial cell injury induced by lactic acidosis in vivo and in vitro. In an in vivo rat peripheral arterial occlusion model induced by lactic acid injection, oral administration of a single dose of 3 mg/kg scymnol significantly inhibited edematous swelling and development of lower limb lesions, including gangrene, and reduced changes in clotting system functions and serum lactate dehydrogenase activity. It had no effect on clotting system functions in sham-operated rats. The structure-activity relationship suggests that the [24R-(+)-5β-cholestane-3α,7α,24,26-pentol] or [3α,7α-dihydroxy-5β-cholanic acid] structure is important for a potent prophylactic effect following oral administration. Intravenous administration of a single dose of 0.3 mg/kg sodium (25S)-scymnol sulfate or scymnol prevented lesion progression as effectively as oral administration of scymnol. Sodium (25S)- scymnol sulfate and ursodeoxycholic acid showed clear protective effects against cultured vascular endothelial cell damage due to lactic acidosis which were dose-dependent. The above results suggest that bile steroids such as scymnol, sodium (25S)-scymnol sulfate, ursodeoxycholic acid, and chenodeoxycholic acid may play a role in protecting endothelial cells against injury caused by lactic acidosis. These compounds are candidates for novel anti-ischemic drugs that act by specifically protecting vascular endothelial cells.
CT Medical Descriptors:
*peripheral occlusive artery disease: DT, drug therapy
*peripheral occlusive artery disease: PC, prevention
gangrene: PC, prevention
structure activity relation
lactate dehydrogenase blood level
prophylaxis
vascular endothelium

cell protection
nonhuman
male
rat
animal experiment
animal model
controlled study
animal tissue
animal cell
oral drug administration
intravenous drug administration
intraperitoneal drug administration
article
Drug Descriptors:
*bile salt: DT, drug therapy
*bile acid: DT, drug therapy
***bile acid conjugate: DT, drug therapy**
*scymnol: DT, drug therapy
lactic acid
lactate dehydrogenase: EC, endogenous compound
ursodeoxycholic acid: DT, drug therapy
argatroban: DT, drug therapy
chenodeoxycholic acid: DT, drug therapy
cholic acid: DT, drug therapy
tauroursodeoxycholic acid: DT, drug therapy
taurochenodeoxycholic acid: DT, drug therapy
taurocholic acid: DT, drug therapy
RN (lactic acid) 113-21-3, 50-21-5; (lactate dehydrogenase) 9001-60-9; (ursodeoxycholic acid) **128-13-2, 2898-95-5**; (argatroban) 74863-84-6; (chenodeoxycholic acid) **474-25-9**; (cholic acid) **32500-01-9, 361-09-1, 81-25-4**; (tauroursodeoxycholic acid) 14605-22-2; (taurochenodeoxycholic acid) 516-35-8; (taurocholic acid) 145-42-6, 59005-70-8, 81-24-3
CO Wako; Tokyo Tanabe; Sigma; Daiichi Pharmaceutical (Japan)

L51 ANSWER 2 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **1999256785** EMBASE
TI Simultaneous determination of ursodeoxycholic acid and its glycine-**conjugate** in serum as phenacyl esters using multidimensional liquid chromatography.
AU Choi S.J.; Jeong C.K.; Lee H.M.; Kim K.; Do K.S.; Lee H.S.
CS S.J. Choi, College of Pharmacy, Wonkwang University, Iksan 570-749, Korea, Republic of
SO Chromatographia, (1999) Vol. 50, No. 1-2, pp. 96-100.
Refs: 25
ISSN: 0009-5893 CODEN: CHRGB7
CY Germany
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 19990812
Last Updated on STN: 19990812
AB A narrowbore high-performance liquid chromatographic (HPLC) method using column switching is described for the simultaneous determination of ursodeoxycholic acid (UDCA) and glyco-UDCA (GUDCA) from serum samples as their phenacyl esters. Serum samples were subjected to a preliminary clean- up using octadecylsilane reversed-phase extraction and derivatized with phenacylbromide. The purification, fractionation and concentration of UDCA and GUDCA from the esterified serum sample were performed on-line by appropriate switching of columns. Limit of detection (LOD) of UDCA and GUDCA were 5 ng and the absolute mean recoveries averaged 84.4 ± 8.2% and 85.2 ±- 8.4%, respectively. This method was successfully applied to the pharmacokinetic study of UDCA in rats and human.

CT Medical Descriptors:
*high performance liquid chromatography
extraction
purification
fractionation
drug blood level
validation process
human
nonhuman
rat
oral drug administration
intravenous drug administration
article
priority journal
Drug Descriptors:
*ursodeoxycholic acid: AD, drug administration
*ursodeoxycholic acid: CR, drug concentration
*ursodeoxycholic acid: DO, drug dose
*ursodeoxycholic acid: PK, pharmacokinetics
*glycine
*ester derivative
*glycoursodeoxycholic acid
silane derivative
bromine derivative
RN (ursodeoxycholic acid) **128-13-2, 2898-95-5**; (glycine) 56-40-6, 6000-43-7, 6000-44-8; (glycoursodeoxycholic acid) **64480-66-6**
CO Sigma (United States)

L51 ANSWER 3 OF 12 EMBASE
on STN
AN **1999046272** EMBASE
TI Inhibition of protein denaturation by fatty acids, bile salts and other natural substances: A new hypothesis for the mechanism of action of fish oil in rheumatic diseases.
AU Saso L.; Valentini G.; Casini M.L.; Mattei E.; Braghiroli L.; Mazzanti G.; Panzironi C.; Grippa E.; Silvestrini B.
CS B. Silvestrini, Inst. Pharmacology and Pharmacognosy, University 'La Sapienza', P.le Aldo Moro 5, 00185 Rome, Italy
SO Japanese Journal of Pharmacology, (1999) Vol. 79, No. 1, pp. 89-99.
Refs: 41
ISSN: 0021-5198 CODEN: JJPAAZ
CY Japan
DT Journal; Article
FS 017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
ED Entered STN: 19990218
Last Updated on STN: 19990218
AB Natural hydrophobic substances like bile salts (cholate, deoxycholate, chenodeoxycholate, lithocholate and their **conjugates** with glycine and taurine), fatty acids (caprylic, capric, lauric, myristic, palmitic, stearic, oleic, linoleic, arachidonic, eicosapentaenoic and docosahexaenoic acid) were much more active (EC50 .simeq. 10-4-10-5 M) than selected amino acids (EC50 > 10-2 M) and inorganic salts (EC50 .simeq. 10-1 M) in inhibiting heat-induced denaturation of human serum albumin in vitro. Fish oil, rich in n-3-polyunsaturated acids such as eicosapentaenoic acid and docosahexaenoic acid, administered p.o. (1 ml/kg) in the rat, protected ex vivo (after 2 hr) serum against heat-induced denaturation more than bendazac, a known antidenaturant drug. Thus, we speculated that the antidenaturant activity of fish oil may be

partly (in addition to the known effect on endogenous eicosanoid composition) responsible for its beneficial effects in rheumatoid arthritis and other rheumatic conditions. In this connection, it is of note that the in vitro antidenaturant activity of fish oil fatty acids was higher than that of known antidenaturant drugs such as bendazac and bindarit and nonsteroidal anti-inflammatory drugs like phenylbutazone and indomethacin which could exert beneficial effects in chronic inflammatory conditions by stabilizing endogenous proteins.

CT Medical Descriptors:
*protein denaturation
*drug mechanism
*rheumatic disease: DT, drug therapy
protein stability
cattle
human
nonhuman
rat
normal human
animal experiment
controlled study
human tissue
animal tissue
oral drug administration
article
Drug Descriptors:
*fatty acid: DV, drug development
*fatty acid: PD, pharmacology
*fish oil: DV, drug development
*fish oil: DT, drug therapy
*fish oil: PD, pharmacology
*bile salt: DV, drug development
*bile salt: PD, pharmacology
cholic acid: CM, drug comparison
cholic acid: DV, drug development
cholic acid: PD, pharmacology
deoxycholic acid: CM, drug comparison
deoxycholic acid: DV, drug development
deoxycholic acid: PD, pharmacology
chenodeoxycholic acid: CM, drug comparison
chenodeoxycholic acid: DV, drug development
chenodeoxycholic acid: PD, pharmacology
lithocholic acid: CM, drug comparison
lithocholic acid: DV, drug development
lithocholic acid: PD, pharmacology
bile acid conjugate: CM, drug comparison
bile acid conjugate: DV, drug development
bile acid conjugate: PD, pharmacology
octanoic acid: CM, drug comparison
octanoic acid: DV, drug development
octanoic acid: PD, pharmacology
decanoic acid: CM, drug comparison
decanoic acid: DV, drug development
decanoic acid: PD, pharmacology
lauric acid: CM, drug comparison
lauric acid: DV, drug development
lauric acid: PD, pharmacology
myristic acid: CM, drug comparison
myristic acid: DV, drug development
myristic acid: PD, pharmacology
palmitic acid: CM, drug comparison
palmitic acid: DV, drug development
palmitic acid: PD, pharmacology
stearic acid: CM, drug comparison
stearic acid: DV, drug development
stearic acid: PD, pharmacology
oleic acid: CM, drug comparison

oleic acid: DV, drug development
oleic acid: PD, pharmacology
linoleic acid: CM, drug comparison
linoleic acid: DV, drug development
linoleic acid: PD, pharmacology
arachidonic acid: CM, drug comparison
arachidonic acid: DV, drug development
arachidonic acid: PD, pharmacology
icosapentaenoic acid: CM, drug comparison
icosapentaenoic acid: DV, drug development
icosapentaenoic acid: PD, pharmacology
docosahexaenoic acid: CM, drug comparison
docosahexaenoic acid: DV, drug development
docosahexaenoic acid: PD, pharmacology
amino acid: CM, drug comparison
amino acid: DV, drug development
amino acid: PD, pharmacology
inorganic salt: CM, drug comparison
inorganic salt: DV, drug development
inorganic salt: PD, pharmacology
human serum albumin
omega 3 fatty acid: CM, drug comparison
omega 3 fatty acid: DV, drug development
omega 3 fatty acid: PD, pharmacology
bendazac: CM, drug comparison
bindarit: CM, drug comparison
phenylbutazone: CM, drug comparison
indometacin: CM, drug comparison
antirheumatic agent: CM, drug comparison
antirheumatic agent: DV, drug development
antirheumatic agent: PD, pharmacology
glycochenodeoxycholic acid: CM, drug comparison
glycochenodeoxycholic acid: DV, drug development
glycochenodeoxycholic acid: PD, pharmacology
unindexed drug
unclassified drug

RN (fish oil) 8016-13-5; (cholic acid) **32500-01-9**, **361-09-1**, **81-25-4**; (deoxycholic acid) **83-44-3**; (chenodeoxycholic acid) **474-25-9**; (lithocholic acid) **434-13-9**; (octanoic acid) 124-07-2, 1984-06-1, 74-81-7; (decanoic acid) 334-48-5, 3398-75-2; (lauric acid) 115-05-9, 143-07-7; (myristic acid) 1715-79-3, 544-63-8; (palmitic acid) 57-10-3; (stearic acid) 57-11-4, 646-29-7; (oleic acid) 112-80-1, 115-06-0; (linoleic acid) 1509-85-9, 2197-37-7, 60-33-3, 822-17-3; (arachidonic acid) 506-32-1, 6610-25-9, 7771-44-0; (icosapentaenoic acid) 25378-27-2, 32839-30-8; (docosahexaenoic acid) 25167-62-8, 32839-18-2; (amino acid) 65072-01-7; (human serum albumin) 9048-49-1; (bendazac) 20187-55-7; (phenylbutazone) 129-18-0, 50-33-9, 8054-70-4; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (glycochenodeoxycholic acid) **640-79-9**

CO Sigma (United States); Merck (Germany)

L51 ANSWER 4 OF 12 EMBASE
on STN

AN **96132330** EMBASE

DN 1996132330

TI Bile acid **conjugation** in early stage cholestatic liver disease before and during treatment with ursodeoxycholic acid.

AU Fracchia M.; Setchell K.D.R.; Crosignani A.; Podda M.; O'Connell N.; Ferraris R.; Hofmann A.F.; Galatola G.

CS Divisione di Gastroenterologia, Ospedale Mauriziano Umberto I, Largo Turati, 62,I-10128 Torino, Italy

SO Clinica Chimica Acta, (1996) Vol. 248, No. 2, pp. 175-185.
ISSN: 0009-8981 CODEN: CCATAR

CY Netherlands

DT Journal; Article

FS 023 Nuclear Medicine

029 Clinical Biochemistry
048 Gastroenterology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 960604
Last Updated on STN: 960604
AB The efficiency of bile acid **conjugation** before and during therapy with 600 mg/day of ursodeoxycholic acid was measured in seven adult patients with early chronic cholestatic liver disease (6 with primary biliary cirrhosis; 1 with primary sclerosing cholangitis). Duodenal bile samples were obtained by aspiration and the proportion of **unconjugated** bile acids was determined using lipophilic anion exchange chromatography to separate bile acid classes, followed by analysis of individual bile acids by gas chromatography-mass spectrometry. The proportion of **conjugated** bile acids was determined by high-performance liquid chromatography. Use of a 99mTc-HIDA recovery marker permitted the absolute mass of **unconjugated** bile acids in the gallbladder to be calculated. **Unconjugated** bile acids comprised 0.4% of total biliary bile acids before and 0.2% during ursodeoxycholic acid therapy, indicating highly efficient **conjugation** of bile acids. During therapy, percentage **unconjugated** ursodeoxycholic acid significantly increased from (mean ± S.D.) 13 ± 13% to 54 ± 12%; $P < 0.002$. When the **unconjugated** and **conjugated** fractions of bile acids were compared, there was an enrichment in **unconjugated** fraction for cholic acid and ursodeoxycholic acid and a depletion for chenodeoxycholic acid both in basal condition and during ursodeoxycholic acid therapy, suggesting that hydrophilic bile acids were **conjugated** less efficiently. During therapy, the **conjugation** efficiency significantly increased for cholic acid and ursodeoxycholic acid. The pretreatment mass of total **unconjugated** bile acids in the gallbladder was (mean ± S.D.) 4.4 ± 3.2 μmol, and was not significantly changed by ursodeoxycholic acid therapy (6.2 ± 3.5 μmol). However, ursodeoxycholic acid therapy caused a significant increase in the mass of **unconjugated** ursodeoxycholic acid. It is concluded that endogenous bile acids and exogenous ursodeoxycholic acid when given at the usual dose are efficiently **conjugated** in patients with early cholestatic liver disease. Despite showing increased biliary **unconjugated** ursodeoxcholic acid during its oral administration, our data do not lend support to the occurrence of hypercholeresis due to cholehepatic shunting of bile acids.
CT Medical Descriptors:
*cholestasis: DT, drug therapy
*liver disease: DT, drug therapy
article
bile composition
clinical article
clinical trial
gas chromatography
high performance liquid chromatography
human
intravenous drug administration
mass spectrometry
oral drug administration
priority journal
Drug Descriptors:
***bile acid conjugate: EC, endogenous compound**
*ursodeoxycholic acid: DT, drug therapy
lidofenin tc 99m
RN (ursodeoxycholic acid) **128-13-2, 2898-95-5**

L51 ANSWER 5 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **95240331** EMBASE
DN 1995240331

TI Tauroursodeoxycholate increases rat liver ursodeoxycholate levels and limits lithocholate formation better than ursodeoxycholate.

AU Rodrigues C.M.P.; Kren B.T.; Steer C.J.; Setchell K.D.R.
CS Department of Pediatrics, Clinical Mass Spectrometry Center, Children's Hospital Medical Center, 3333 Burnet Avenue,Cincinnati, OH 45229, United States

SO Gastroenterology, (1995) Vol. 109, No. 2, pp. 564-572.
ISSN: 0016-5085 CODEN: GASTAB
CY United States
DT Journal; Article
FS 037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 950906
Last Updated on STN: 950906

AB Background and Aims: To explain the greater hepatoprotective effect of tauroursodeoxycholic acid vs. ursodeoxycholic acid, the absorption, hepatic enrichment, and biotransformation of these bile acids (250 mg/day) were compared in rats. Methods: Bile acids were determined in intestinal contents, feces, urine, plasma, and liver by gas chromatography-mass spectrometry. Results: The concentration of ursodeoxycholate in the liver of animals administered tauroursodeoxycholic acid (175 ± 29 nmol/g) was greater ($P < 0.05$) than in animals administered ursodeoxycholic acid (79 ± 19 nmol/g). Hepatic lithocholate was substantially higher after ursodeoxycholic acid administration (21 ± 10 nmol/g) than after tauroursodeoxycholic acid administration (12 ± 1 nmol/g). A concomitant reduction in the proportion of hydrophobic bile acids occurred that was greatest during tauroursodeoxycholic acid administration. In the intestinal tract, the mass of ursodeoxycholate and its specific metabolites was greater in rats administered tauroursodeoxycholic acid (27.2 mg) than those administered ursodeoxycholic acid (13.2 mg). In feces, the proportion of lithocholate was 21.9% ± 4.9% and 5.4% ± 4.0% after ursodeoxycholic acid and tauroursodeoxycholic acid administration, respectively. Conclusions: Compared with ursodeoxycholic acid, tauroursodeoxycholic acid induces a greater decrease in the percent composition of more hydrophobic bile acids within the pool, limits lithocholate formation, and increases hepatic ursodeoxycholate concentration. These differences are explained by increased hepatic extraction and reduced intestinal biotransformation and not by enhanced absorption of the amidated species.

CT Medical Descriptors:
*bile acid metabolism
*biotransformation
*liver protection
amidation
animal experiment
animal tissue
article
blood level
controlled study
drug mechanism
feces level
gas chromatography
hydrophobicity
intestine absorption
male
mass spectrometry
nonhuman
oral drug administration
priority journal
rat
urine level
Drug Descriptors:
*bile acid: EC, endogenous compound
*lithocholic acid: EC, endogenous compound

*tauroursodeoxycholic acid: CM, drug comparison
*tauroursodeoxycholic acid: PD, pharmacology
*ursodeoxycholic acid: CM, drug comparison
*ursodeoxycholic acid: PD, pharmacology
bile acid conjugate: EC, endogenous compound
RN (lithocholic acid) **434-13-9**; (tauroursodeoxycholic acid) 14605-22-2; (ursodeoxycholic acid) **128-13-2, 2898-95-5**
CO Sigma (United States)

L51 ANSWER 6 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **94299511** EMBASE
DN 1994299511
TI Effect of a medium dose of ursodeoxycholic acid with or without taurine supplementation on the nutritional status of patients with cystic fibrosis: A randomized, placebo-controlled, crossover trial.
AU Merli M.; Bertasi S.; Servi R.; Diamanti S.; Martino F.; De Santis A.; Goffredo F.; Quattrucci S.; Antonelli M.; Angelico M.
CS II Cattedra di Gastroenterologia, Viale dell'Universita, 37,00185 Rome, Italy
SO Journal of Pediatric Gastroenterology and Nutrition, (1994) Vol. 19, No. 2, pp. 198-203.
ISSN: 0277-2116 CODEN: JPGND6
CY United States
DT Journal; Article
FS 007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 941027
Last Updated on STN: 941027
AB Ursodeoxycholic acid administration has been reported to improve cholestasis and inflammatory activity in primary biliary cirrhosis and, in an uncontrolled study, also in young adults with cystic fibrosis (CF) and chronic cholestasis. As an improvement in nutritional status was also observed in these young adult patients, we investigated whether the administration of a medium dose of ursodeoxycholic acid ameliorates the nutritional status of malnourished young adult CF patients with chronic liver disease. The study included 51 patients (27 male patients and 24 female patients; age range, 8-32 years; median, 14) with body mass percentiles <90%. Patients were randomly assigned to receive either ursodeoxycholic acid (10- 12 mg/kg/day) alone or with taurine (18-22 mg/kg/day). Patients were followed in a crossover fashion within each group; 6 months of treatment was randomly alternated with 6 months of placebo. Nine patients dropped out before concluding the study. Liver function tests, nutritional status, and coefficients of fat absorption were determined at entry and after each 6 months of placebo or treatment. Nutritional status and fat absorption were not significantly modified by either treatment. Liver function tests improved after ursodeoxycholic acid administration only in patients with concomitant chronic liver disease. Our findings indicate that 6 months of therapy with a medium dose of ursodeoxycholic acid, either alone or with taurine, does not improve the nutritional status of young malnourished CF patients. Higher doses given for longer periods might be worth investigating.
CT Medical Descriptors:
*cholestasis: DT, drug therapy
*cystic fibrosis: CN, congenital disorder
*diet supplementation
*nutritional status
adolescent
article
body mass
child
clinical trial
controlled study

crossover procedure
dose response
drug efficacy
drug mixture
enzyme therapy
female
human
lipid absorption
liver function test
major clinical study
male
malnutrition: TH, therapy
malnutrition: CO, complication
oral drug administration
pancreas insufficiency: DT, drug therapy
pancreas insufficiency: CO, complication
priority journal
randomized controlled trial
Drug Descriptors:
*taurine: DT, drug therapy
*taurine: CB, drug combination
*taurine: CT, clinical trial
*ursodeoxycholic acid: CT, clinical trial
*ursodeoxycholic acid: DT, drug therapy
*ursodeoxycholic acid: DO, drug dose
*ursodeoxycholic acid: CB, drug combination
alanine aminotransferase: EC, endogenous compound
alkaline phosphatase: EC, endogenous compound
amylase: DT, drug therapy
amylase: CB, drug combination
aspartate aminotransferase: EC, endogenous compound
bile acid conjugate: EC, endogenous compound
ceruletide
ceruletide diethylamine
feces lipid
gamma glutamyltransferase: EC, endogenous compound
pancrelipase: DT, drug therapy
placebo
tauroursodeoxycholic acid: EC, endogenous compound
triacylglycerol lipase: CB, drug combination
triacylglycerol lipase: DT, drug therapy
trypsin: DT, drug therapy
trypsin: CB, drug combination
vitamin

RN (taurine) 107-35-7; (ursodeoxycholic acid) 128-13-2, 2898-95-5; (alanine aminotransferase) 9000-86-6, 9014-30-6; (alkaline phosphatase) 9001-78-9; (amylase) 9000-90-2, 9000-92-4, 9001-19-8; (aspartate aminotransferase) 9000-97-9; (ceruletide) 17650-98-5; (ceruletide diethylamine) 71247-25-1; (gamma glutamyltransferase) 85876-02-4; (pancrelipase) 71060-52-1, 83869-36-7; (tauroursodeoxycholic acid) 14605-22-2; (triacylglycerol lipase) 9001-62-1; (trypsin) 9002-07-7
CN (1) Takus
CO (1) Farmitalia carlo erba (Italy)

L51 ANSWER 7 OF 12 EMBASE
on STN
AN **92292458** EMBASE
DN 1992292458
TI Effect of ursodeoxycholic acid on the masses of biliary lipids and alkaline phosphatase within the gallbladder in chronic cholestatic liver disease.
AU Fracchia M.; Ferraris R.; Petrarulo M.; Secreto P.; Dunn T.; Galatola G.
CS Divisione di Gastroenterologia, Ospedale Mauriziano Umberto I, Largo Turati 62,I-10128 Torino, Italy
SO European Journal of Gastroenterology and Hepatology, (1992) Vol. 4, No.

10, pp. 843-848.
ISSN: 0954-691X CODEN: EJGHES
CY United Kingdom
DT Journal; Conference Article
FS 030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LA English
SL English
ED Entered STN: 921025
Last Updated on STN: 921025
AB Objectives: To verify whether the improvement of the cholestatic indices caused by ursodeoxycholic acid administered for chronic intrahepatic cholestasis is due to a dilution or a removal of the hydrophobic bile acids in the bile. To assess the effect of ursodeoxycholic acid on the masses in the gallbladder of other biliary lipids and alkaline phosphatase. Design: Open prospective study. Methods: Measurement of the masses of total bile acids, bile acid **conjugates**, cholesterol, phospholipid and alkaline phosphatase within the gallbladder in the fasting state before and after 4-6 weeks of therapy with 600 mg per day oral ursodeoxycholic acid in eight patients with chronic cholestatic liver disease. Results: Ursodeoxycholic acid caused a significant increase in the bile acid mass (from 1976 ± 593 to 4562 ± 1474 μmol; P < 0.02), that was entirely due to an increased mass of its **conjugates** (from 35 ± 20 to 1623 ± 768 μmol; P < 0.05), whereas the masses of all the other bile acid **conjugates** were not modified during therapy. In all eight patients, serum alkaline phosphatase concentration decreased during ursodeoxycholic acid therapy, whereas the alkaline phosphatase mass within the gallbladder increased, from 16 ± 3 IU to 35 ± 9 IU (P < 0.02). There was no change in the cholesterol and phospholipid masses. Conclusion: Our results indicate that the mechanism of action of ursodeoxycholic acid in chronic intrahepatic cholestasis is not mediated via a reduction of the hydrophobic bile acids handled by the liver, though these are diluted out by ursodeoxycholic acid. The finding of an increased mass of alkaline phosphatase in the gallbladder is probably due to the well known choleretic effect of ursodeoxycholic acid.
CT Medical Descriptors:
*cholestasis: DT, drug therapy
*chronic liver disease: DT, drug therapy
*gallbladder
*lipid bile level
adult
aged
alkaline phosphatase blood level
clinical article
conference paper
female
human
male
oral drug administration
primary biliary cirrhosis: DT, drug therapy
primary sclerosing cholangitis: DT, drug therapy
prospective study
Drug Descriptors:
*alkaline phosphatase: EC, endogenous compound
*ursodeoxycholic acid: DT, drug therapy
*ursodeoxycholic acid: PD, pharmacology
bile acid conjugate: EC, endogenous compound
cholesterol: EC, endogenous compound
phospholipid: EC, endogenous compound
RN (alkaline phosphatase) 9001-78-9; (ursodeoxycholic acid) **128-13-2**, **2898-95-5**; (cholesterol) 57-88-5
CN Deursil
CO Labaz (Italy)

L51 ANSWER 8 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 90226900 EMBASE
DN 1990226900
TI Prevention of ursodeoxycholate hepatotoxicity in the rabbit by **conjugation** with N-methyl amino acids.
AU Schmassmann A.; Hofmann A.F.; Angellotti M.A.; Ton-Nu H.-T.; Schteingart C.D.; Clerici C.; Rossi S.S.; Rothschild M.A.; Cohen B.I.; Stenger R.J.; Mosbach E.H.
CS Lipid Laboratory, Department of Surgery, Beth Israel Medical Center, 10 Nathan D. Perlman Place,New York, NY 10003, United States
SO Hepatology, (1990) Vol. 11, No. 6, pp. 989-996.
ISSN: 0270-9139 CODEN: HPTLD
CY United States
DT Journal; Article
FS 048 Gastroenterology
052 Toxicology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 911213
Last Updated on STN: 911213
AB The effect of dietary administration of four different amino acid (N-acyl) **conjugates** of ursodeoxycholic acid on biliary bile acid composition, liver tests and hepatic morphology by light microscopy was examined in the rabbit. Each group of four to five rabbits received a chow diet supplemented with a single **conjugate** of ursodeoxycholic acid ursodeoxycholyl-glycine, ursodeoxycholyl-sarcosine, ursodeoxycholyl-taurine or ursodeoxycholyl-N-methyltaurine for 3 wks at a dose of 50 mg/kg/day; a control group received chow alone. After 3 wks of feeding, animals receiving ursodeoxycholyl-glycine or ursodeoxycholyl-taurine had hepatotoxicity associated with abnormal liver tests. Lithocholic acid made up 11% ± 2.7% of biliary bile acids in the ursodeoxycholyl-glycine and 10% ± 2.2% in the ursodeoxycholyl-taurine group. In contrast, animals receiving ursodeoxycholyl-sarcosine or ursodeoxycholyl-N-methyltaurine had neither hepatotoxicity nor abnormal liver tests and the proportion of lithocholic acid in biliary bile acids increased much less. Complementary studies showed that ursodeoxycholyl-sarcosine and ursodeoxycholyl-N-methyltaurine were not biotransformed during hepatic transport and were resistant to **deconjugation** and dehydroxylation in the rabbit. These experiments indicate that the N-methyl amino acid **conjugates** of ursodeoxycholic acid are nontoxic in the rabbit and resist **deconjugation** and dehydroxylation. Such resistance decreases formation of lithocholic acid in the colon, thus reducing its accumulation and consequent induction of hepatotoxicity.
CT Medical Descriptors:
***conjugation**
*liver toxicity: PC, prevention
drug conjugation
rabbit
animal experiment
nonhuman
male
oral drug administration
article
priority journal
Drug Descriptors:
*amino acid
*ursodeoxycholic acid: TO, drug toxicity
RN (amino acid) 65072-01-7; (ursodeoxycholic acid) **128-13-2**, **2898-95-5**
CO Diamalt aktiengeschellschaft (Germany)

L51 ANSWER 9 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 89150062 EMBASE
DN 1989150062
TI The rapid evaluation of intestinal bacterial growth using a **conjugate** of ursodeoxycholic acid with para-aminobenzoic acid.
AU Maeda Y.; Takahashi M.; Tashiro H.; Akazawa F.
CS Department of Pharmacy, Chugoku Rosai Hospital, Hiroshima 737-01, Japan
SO Journal of Pharmacobio-Dynamics, (1989) Vol. 12, No. 5, pp. 272-280.
ISSN: 0386-846X CODEN: JOPHDQ
CY Japan
DT Journal
FS 030 Pharmacology
037 Drug Literature Index
LA English
ED Entered STN: 911212
Last Updated on STN: 911212
CT Medical Descriptors:
*bacterial count
*bacterial growth
*blind loop syndrome
*intestine flora
animal model
choloylglycine hydrolase
rat
microorganism
animal experiment
nonhuman
male
oral drug administration
Drug Descriptors:
bile acid
4 ursodeoxycholamidobenzoic acid
clindamycin
glycocholic acid
kanamycin
paromomycin
polymyxin b
tinidazole
vancomycin
unclassified drug
RN (clindamycin) 18323-44-9; (glycocholic acid) 475-31-0; (kanamycin) 11025-66-4, 61230-38-4, 8063-07-8; (paromomycin) 11035-13-5, 1263-89-4, 1390-73-4, 51795-47-2, 54597-56-7, 7542-37-2, 84420-34-8; (polymyxin b) 1404-26-8, 1405-20-5; (tinidazole) 19387-91-8; (vancomycin) 1404-90-6, 1404-93-9
CO Wako pure chemical industry (Japan); Shionogi (Japan); Upjohn (Japan); Meiji seika kaisha (Japan); Kyowa hakko kogyo (Japan); Pfizer (Japan); Tokyo tanabe (Japan)

L51 ANSWER 10 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 88276787 EMBASE
DN 1988276787
TI HPLC assay of **conjugated** bile acids in gastric juice during ursodeoxycholic acid (Deursil®) therapy of bile reflux gastritis.
AU Scalia S.; Pazzi P.; Stabellini G.; Guarneri M.
CS Department of Pharmaceutical Sciences, University of Ferrara, 44100 Ferrara, Italy
SO Journal of Pharmaceutical and Biomedical Analysis, (1988) Vol. 6, No. 6-8, pp. 911-917.
ISSN: 0731-7085 CODEN: JPBADA
CY United Kingdom
DT Journal
FS 029 Clinical Biochemistry
048 Gastroenterology
037 Drug Literature Index
LA English

SL English
ED Entered STN: 911211
Last Updated on STN: 911211
AB A rapid high-performance liquid chromatographic method for the direct assay of the taurine and glycine **conjugated** bile acids in human gastric juice is described. After extraction with Sep-Pak C18 cartridges, compounds are baseline resolved on a reversed-phase column and detected by UV absorption. The procedure is linear from 10 μmol l-1 to 1200 μmol l-1, with recovery rates ranging from 87 to 100%. The present method is applicable to the quantification of bile acid **conjugates** in human gastric bile with satisfactory sensitivity, selectivity and precision. Intragastric bile acid compositions in 10 patients with bile reflux gastritis during Deursil® or placebo treatment are presented.
CT Medical Descriptors:
*bile reflux
*gastritis: DI, diagnosis
*gastritis: DT, drug therapy
*high performance liquid chromatography
*stomach juice
clinical article
human cell
human
methodology
oral drug administration
Drug Descriptors:
***bile acid conjugate**
*ursodeoxycholic acid: DT, drug therapy
RN (ursodeoxycholic acid) 128-13-2, 2898-95-5
CN (1) Deursil
CO (1) Gipharmex (Italy)

L51 ANSWER 11 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 85080967 EMBASE
DN 1985080967
TI Synthesis, intestinal absorption and metabolism of sarcosine **conjugated** ursodeoxycholic acid.
AU Kimura M.; Hatono S.; Une M.; et al.
CS Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Minami-Ku, Hiroshima 734, Japan
SO Steroids, (1984) Vol. 43, No. 6, pp. 677-687.
CODEN: STEDAM
CY United States
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
023 Nuclear Medicine
048 Gastroenterology
LA English
ED Entered STN: 911210
Last Updated on STN: 911210
AB Sarcosine **conjugated** ursodeoxycholic acid (SUDC) was synthesized and its intestinal absorption and metabolism were studied in rat and hamster. Intestinal absorption study using bile fistula rat shows that more than 90% of SUDC administered intraduodenally was excreted in the bile within 24 hr. No change of the administered bile acid was seen during the absorption from the intestine, the passage of the liver, and the excretion into the bile. When [24-14C]SUDC and [11,12-3H2]-ursodeoxycholic acid were administered orally to a hamster, more than 95% of both the administered 14C and 3H were recovered from the feces within 6 days. Most (77%) of the fecal 14C-labeled compound was SUDC, whereas 95% of the fecal 3H-labeled compound was **unconjugated** lithocholic acid. These results indicate that SUDC, unlike taurine or glycine **conjugated** bile acid, resists bacterial **deconjugation** and 7-dehydroxylation.
CT Medical Descriptors:

*bile acid conjugation
*drug absorption
*drug bile level
*drug distribution
*drug elimination
*drug feces level
*drug identification
*drug metabolism
*drug monitoring
*drug synthesis
*drug tissue level
*high performance liquid chromatography
*infrared spectrometry
*intestine absorption
*ion exchange chromatography
*nuclear magnetic resonance
*sarcoursodeoxycholic acid
*sarcoursodeoxycholic acid c 14
*ursodeoxycholic acid c 14
*ursodeoxycholic acid h 3
metabolism
priority journal
drug analysis
oral drug administration
nonhuman
rat
small intestine
liver
animal experiment
Drug Descriptors:
*lithocholic acid
*sarcosine
radioisotope
RN (lithocholic acid) 434-13-9; (sarcosine) 107-97-1
CO Daiichi; Nen

L51 ANSWER 12 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 84147710 EMBASE
DN 1984147710
TI Effect of ursodeoxycholate and its taurine conjugate on bile acid synthesis and cholesterol absorption.
AU Hardison W.G.M.; Grundy S.M.
CS Department of Medicine, Veterans Administration Medical Center, San Diego, TX, United States
SO Gastroenterology, (1984) Vol. 87, No. 1, pp. 130-135.
CODEN: GASTAB
CY United States
DT Journal
FS 037 Drug Literature Index
048 Gastroenterology
006 Internal Medicine
029 Clinical Biochemistry
003 Endocrinology
023 Nuclear Medicine
LA English
ED Entered STN: 911210
Last Updated on STN: 911210
AB Six male subjects with normal gastroenterologic function were studied to determine the effects of ursodeoxycholic (15 mg/kg·day) and tauroursodeoxycholic (20 mg/kg·day) acid feeding on bile acid synthesis and cholesterol absorption. Each bile acid was fed for 1 mo and withheld for the next month. Subjects remained on a metabolic ward and consumed a constant diet of 500 mg of cholesterol mixed with solid and liquid formulas. Before the study started, each subject received 50 μCi of [4-14C]cholesterol intravenously. During the study, stools were

collected for the determination of 24-h fecal acidic and neutral sterol excretion, and blood was drawn twice weekly for determination of serum cholesterol specific activity. At the end of each month an intestinal perfusion study was performed to measure total bile acid pool size and hourly biliary secretion rates of cholesterol, phospholipid, and bile acid. From these data, the percentage of cholesterol absorption and total endogenous bile acid synthesis could be calculated. Neither ursodeoxycholic nor tauroursodeoxycholic acid feeding decreased endogenous bile acid synthesis. During bile acid feeding periods, the percentage of cholesterol absorption was decreased.

CT Medical Descriptors:
*cholesterol c 14
*drug efficacy
*intestine absorption
oral drug administration
human
normal human
liver
human experiment
Drug Descriptors:
*bile acid
*cholesterol
*tauroursodeoxycholic acid
*ursodeoxycholic acid
radioisotope

RN (cholesterol) 57-88-5; (tauroursodeoxycholic acid) 14605-22-2; (ursodeoxycholic acid) **128-13-2, 2898-95-5**

CO Nen (United States)

=> b biosis
FILE 'BIOSIS' ENTERED AT 09:39:27 ON 24 JUN 2005
Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 23 June 2005 (20050623/ED)

FILE RELOADED: 19 October 2003.

=> d all l60 tot

L60 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:31809 BIOSIS
DN PREV200300031809
TI Absorption of biologically active peptide hormones from the small intestine of rat.
AU **Wheeler, S.**; McGinn, B. J.; **Lucas, M. L.**; **Morrison, J. D.** [Reprint Author]
CS University of Glasgow, West Medical Building, Glasgow, G12 8QQ, UK
SO Acta Physiologica Scandinavica, (November 2002) Vol. 176, No. 3, pp. 203-213. print.
ISSN: 0001-6772 (ISSN print).
DT Article
LA English
ED Entered STN: 8 Jan 2003
Last Updated on STN: 8 Jan 2003
AB Absorption of the 4, 10 and 34 amino acid forms of gastrin from the small intestine has been investigated in anaesthetized rats. The method of assessment of successful absorption of the hormone into the systemic circulation was when the amount of acid secreted by the stomach over consecutive 15-min periods was increased. When the natural hormones were infused into the ileum in a relatively high dose, there was no increase in gastric acid secretion, indicating that they had not been absorbed. Each

of the forms of gastrin was **conjugated** at the free amino terminus to the carboxyl group of cholic acid. Subsequent infusion of the **conjugated** form of gastrin into the ileum, this time in relatively low doses, resulted in substantial and prolonged increases in gastric acid secretion, indicating that these hormones had been successfully absorbed. In addition, **conjugation** of the 10 and 34 amino acid forms of gastrin with cholic acid was shown to increase markedly the potency in evoking an increase in gastric acid secretion in response to intravenous injection of the hormone. Absorption of the gastrin **conjugates** was specific to the ileum thus indicating that they had been absorbed through the bile salt transporters.

CC Biochemistry studies - General 10060
Digestive system - Physiology and biochemistry 14004

IT Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation)

IT Parts, Structures, & Systems of Organisms
ileum: digestive system; small intestine: digestive system; stomach: digestive system

IT Chemicals & Biochemicals
bile salt transporters; biologically active peptide hormones: absorption; cholic acid; gastrin **conjugates**: absorption

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Wistar rat (common): male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN **81-25-4** (cholic acid)

=> b home
FILE 'HOME' ENTERED AT 09:39:33 ON 24 JUN 2005

=>